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(54) Title: NOVEL COMPOUNDS

(57) Abstract: Polypeptides and polynucleotides of the genes set forth in Table I and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing polypeptides and polynucleotides of the genes set forth in Table I in diagnostic assays.

Novel Compounds

Field of Invention

This invention relates to newly identified polypeptides and polynucleotides encoding such polypeptides, to their use in diagnosis and in identifying compounds that may be agonists, antagonists that are potentially useful in therapy, and to production of such polypeptides and polynucleotides. The polynucleotides and polypeptides of the present invention also relate to proteins with signal sequences which allow them to be secreted extracellularly or membrane-associated (hereinafter often referred collectively as secreted proteins or secreted polypeptides).

Background of the Invention

The drug discovery process is currently undergoing a fundamental revolution as it embraces "functional genomics", that is, high throughput genome- or gene-based biology. This approach as a means to identify genes and gene products as therapeutic targets is rapidly superseding earlier approaches based on "positional cloning". A phenotype, that is a biological function or genetic disease, would be identified and this would then be tracked back to the responsible gene, based on its genetic map position.

Functional genomics relies heavily on high-throughput DNA sequencing technologies and the various tools of bioinformatics to identify gene sequences of potential interest from the many molecular biology databases now available. There is a continuing need to identify and characterise further genes and their related polypeptides/proteins, as targets for drug discovery.

Proteins and polypeptides that are naturally secreted into blood, lymph and other body fluids, or secreted into the cellular membrane are of primary interest for pharmaceutical research and development. The reason for this interest is the relative ease to target protein therapeutics into their place of action (body fluids or the cellular membrane). The natural pathway for protein secretion into extracellular space is the endoplasmic reticulum in eukaryotes and the inner membrane in prokaryotes (Palade, 1975, Science, 189, 347; Milstein, Brownlee, Harrison, and Mathews, 1972, Nature New Biol., 239, 117; Blobel, and Dobberstein, 1975, J. Cell. Biol., 67, 835). On the other hand, there is no known natural pathway for exporting a protein from the exterior of the cells into the cytosol (with the exception of pinocytosis, a mechanism of snake venom toxin intrusion into cells). Therefore targeting protein therapeutics into cells poses extreme difficulties.

The secreted and membrane-associated proteins include but are not limited

to all peptide hormones and their receptors (including but not limited to insulin, growth hormones, chemokines, cytokines, neuropeptides, integrins, kallikreins, lamins, melanins, natriuretic hormones, neuropsin, neurotropins, pituitiary hormones, pleiotropins, prostaglandins, secretogranins, selectins, thromboglobulins, thymosins), the breast and colon cancer gene products, leptin, the obesity gene protein and its receptors, serum albumin, superoxide dismutase, spliceosome proteins, 7TM (transmembrane) proteins also called as G-protein coupled receptors, immunoglobulins, several families of serine proteinases (including but not limited to proteins of the blood coagulation cascade, digestive enzymes), deoxyribonuclease I, etc.

Therapeutics based on secreted or membrane-associated proteins approved by FDA or foreign agencies include but are not limited to insulin, glucagon, growth hormone, chorionic gonadotropin, follicle stimulating hormone, luteinizing hormone, calcitonin, adrenocorticotropic hormone (ACTH), vasopressin, interleukines, interferones, immunoglobulins, lactoferrin (diverse products marketed by several companies), tissue-type plasminogen activator (Alteplase by Genentech), hyaulorindase (Wydase by Wyeth-Ayerst), dornase alpha (Pulmozyme\ by Genentech), Chymodiactin (chymopapain by Knoll), alglucerase (Ceredase by Genzyme), streptokinase (Kabikinase by Pharmacia) (Streptase by Astra), etc. This indicates that secreted and membrane-associated proteins have an established, proven history as therapeutic targets. Clearly, there is a need for identification and characterization of further secreted and membrane-associated proteins which can play a role in preventing, ameliorating or correcting dysfunction or disease, including but not limited to diabetes, breast-, prostate-, colon cancer and other malignant tumors, hyper- and hypotension, obesity, bulimia, anorexia, growth abnormalities, asthma, manic depression, dementia, delirium, mental retardation, Huntington's disease, Tourette's syndrome, schizophrenia, growth, mental or sexual development disorders, and dysfunctions of the blood cascade system including those leading to stroke. The proteins of the present invention which include the signal sequences are also useful to further elucidate the mechanism of protein transport which at present is not entirely understood, and thus can be used as research tools.

Summary of the Invention

The present invention relates to particular polypeptides and polynucleotides of the genes set forth in Table I, including recombinant materials and methods for their production.

Such polypeptides and polynucleotides are of interest in relation to methods of treatment of certain diseases, including, but not limited to, the diseases set forth in Tables III and V, hereinafter referred to as "diseases of the invention". In a further aspect, the invention relates to methods for identifying agonists and antagonists (*e.g.*, inhibitors) using the materials provided by the invention, and treating conditions associated with imbalance of polypeptides and/or polynucleotides of the genes set forth in Table I with the identified compounds. In still a further aspect, the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels the genes set forth in Table I. Another aspect of the invention concerns a polynucleotide comprising any of the nucleotide sequences set forth in the Sequence Listing and a polypeptide comprising a polypeptide encoded by the nucleotide sequence. In another aspect, the invention relates to a polypeptide comprising any of the polypeptide sequences set forth in the Sequence Listing and recombinant materials and methods for their production. Another aspect of the invention relates to methods for using such polypeptides and polynucleotides. Such uses include the treatment of diseases, abnormalities and disorders (hereinafter simply referred to as diseases) caused by abnormal expression, production, function and or metabolism of the genes of this invention, and such diseases are readily apparent by those skilled in the art from the homology to other proteins disclosed for each attached sequence. In still another aspect, the invention relates to methods to identify agonists and antagonists using the materials provided by the invention, and treating conditions associated with the imbalance with the identified compounds. Yet another aspect of the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels of the secreted proteins of the present invention.

Description of the Invention

In a first aspect, the present invention relates to polypeptides the genes set forth in Table I. Such polypeptides include:

(a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in the Sequence Listing, herein when referring to polynucleotides or polypeptides of the Sequence Listing, a reference is also made to the Sequence Listing referred to in the Sequence Listing;

(b) an isolated polypeptide comprising a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(c) an isolated polypeptide comprising a polypeptide sequence set forth in the Sequence Listing;

(d) an isolated polypeptide having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(e) a polypeptide sequence set forth in the Sequence Listing; and

(f) an isolated polypeptide having or comprising a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing;

(g) fragments and variants of such polypeptides in (a) to (f).

Polypeptides of the present invention are believed to be members of the gene families set forth in Table II . They are therefore of therapeutic and diagnostic interest for the reasons set forth in Tables III and V. The biological properties of the polypeptides and polynucleotides of the genes set forth in Table I are hereinafter referred to as "the biological activity" of polypeptides and polynucleotides of the genes set forth in Table I. Preferably, a polypeptide of the present invention exhibits at least one biological activity of the genes set forth in Table I.

Polypeptides of the present invention also include variants of the aforementioned polypeptides, including all allelic forms and splice variants. Such polypeptides vary from the reference polypeptide by insertions, deletions, and substitutions that may be conservative or non-conservative, or any combination thereof. Particularly preferred variants are those in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acids are inserted, substituted, or deleted, in any combination.

Preferred fragments of polypeptides of the present invention include an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids from an amino acid sequence set forth in the Sequence Listing, or an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids truncated or deleted from an amino acid sequence set forth in the Sequence Listing. Preferred fragments are biologically active fragments that mediate the biological activity of polypeptides and polynucleotides of the genes set forth in Table I, including those with a similar activity or an improved activity, or with a decreased undesirable activity. Also preferred are those fragments that are antigenic or immunogenic in an animal, especially in a human.

Fragments of a polypeptide of the invention may be employed for producing the corresponding full-length polypeptide by peptide synthesis; therefore, these variants may be employed as intermediates for producing the full-length polypeptides of the invention. A polypeptide of the present invention may be in the form of the "mature" protein or may be a

part of a larger protein such as a precursor or a fusion protein. It is often advantageous to include an additional amino acid sequence that contains secretory or leader sequences, pro-sequences, sequences that aid in purification, for instance multiple histidine residues, or an additional sequence for stability during recombinant production.

Polypeptides of the present invention can be prepared in any suitable manner, for instance by isolation form naturally occurring sources, from genetically engineered host cells comprising expression systems (*vide infra*) or by chemical synthesis, using for instance automated peptide synthesizers, or a combination of such methods. Means for preparing such polypeptides are well understood in the art.

In a further aspect, the present invention relates to polynucleotides of the genes set forth in Table I. Such polynucleotides include:

(a) an isolated polynucleotide comprising a polynucleotide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide sequence set forth in the Sequence Listing;

(b) an isolated polynucleotide comprising a polynucleotide set forth in the Sequence Listing;

(c) an isolated polynucleotide having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide set forth in the Sequence Listing;

(d) an isolated polynucleotide set forth in the Sequence Listing;

(e) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(f) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing;

(g) an isolated polynucleotide having a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(h) an isolated polynucleotide encoding a polypeptide set forth in the Sequence Listing;

(i) an isolated polynucleotide having or comprising a polynucleotide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polynucleotide sequence set forth in the Sequence Listing;

(j) an isolated polynucleotide having or comprising a polynucleotide sequence encoding a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing; and

polynucleotides that are fragments and variants of the above mentioned polynucleotides or that are complementary to above mentioned polynucleotides, over the entire length thereof.

Preferred fragments of polynucleotides of the present invention include an isolated polynucleotide comprising an nucleotide sequence having at least 15, 30, 50 or 100 contiguous nucleotides from a sequence set forth in the Sequence Listing, or an isolated polynucleotide comprising a sequence having at least 30, 50 or 100 contiguous nucleotides truncated or deleted from a sequence set forth in the Sequence Listing.

Preferred variants of polynucleotides of the present invention include splice variants, allelic variants, and polymorphisms, including polynucleotides having one or more single nucleotide polymorphisms (SNPs).

Polynucleotides of the present invention also include polynucleotides encoding polypeptide variants that comprise an amino acid sequence set forth in the Sequence Listing and in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acid residues are substituted, deleted or added, in any combination.

In a further aspect, the present invention provides polynucleotides that are RNA transcripts of the DNA sequences of the present invention. Accordingly, there is provided an RNA polynucleotide that:.

(a) comprises an RNA transcript of the DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(b) is a RNA transcript of a DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(c) comprises an RNA transcript of a DNA sequence set forth in the Sequence Listing; or

(d) is a RNA transcript of a DNA sequence set forth in the Sequence Listing; and RNA polynucleotides that are complementary thereto.

The polynucleotide sequences set forth in the Sequence Listing show homology with the polynucleotide sequences set forth in Table II. A polynucleotide sequence set forth in the Sequence Listing is a cDNA sequence that encodes a polypeptide set forth in the Sequence Listing. A polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing may be identical to a polypeptide encoding a sequence set forth in the Sequence Listing or it may be a sequence other than a sequence set forth in the Sequence Listing, which, as a result of the redundancy (degeneracy) of the genetic code, also encodes a polypeptide set forth in the Sequence Listing. A polypeptide of a sequence set forth in the Sequence Listingis related to other proteins of the gene families set forth in Table II, having

homology and/or structural similarity with the polypeptides set forth in Table II. Preferred polypeptides and polynucleotides of the present invention are expected to have, *inter alia*, similar biological functions/properties to their homologous polypeptides and polynucleotides. Furthermore, preferred polypeptides and polynucleotides of the present invention have at least one activity of the genes set forth in Table I.

Polynucleotides of the present invention may be obtained using standard cloning and screening techniques from a cDNA library derived from mRNA from the tissues set forth in Table IV (see for instance, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). Polynucleotides of the invention can also be obtained from natural sources such as genomic DNA libraries or can be synthesized using well known and commercially available techniques.

When polynucleotides of the present invention are used for the recombinant production of polypeptides of the present invention, the polynucleotide may include the coding sequence for the mature polypeptide, by itself, or the coding sequence for the mature polypeptide in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or prepro- protein sequence, or other fusion peptide portions. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain preferred embodiments of this aspect of the invention, the marker sequence is a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, Proc Natl Acad Sci USA (1989) 86:821-824, or is an HA tag. A polynucleotide may also contain non-coding 5' and 3' sequences, such as transcribed, non-translated sequences, splicing and polyadenylation signals, ribosome binding sites and sequences that stabilize mRNA.

Polynucleotides that are identical, or have sufficient identity to a polynucleotide sequence set forth in the Sequence Listing, may be used as hybridization probes for cDNA and genomic DNA or as primers for a nucleic acid amplification reaction (for instance, PCR). Such probes and primers may be used to isolate full-length cDNAs and genomic clones encoding polypeptides of the present invention and to isolate cDNA and genomic clones of other genes (including genes encoding paralogs from human sources and orthologs and paralogs from other species) that have a high sequence similarity to sequences set forth in the Sequence Listing, typically at least 95% identity. Preferred probes and primers will generally comprise at least 15 nucleotides, preferably, at least 30 nucleotides and may have at least 50, if not at least 100 nucleotides. Particularly preferred probes will have between

30 and 50 nucleotides. Particularly preferred primers will have between 20 and 25 nucleotides.

A polynucleotide encoding a polypeptide of the present invention, including homologs from other species, may be obtained by a process comprising the steps of screening a library under stringent hybridization conditions with a labeled probe having a sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides; and isolating full-length cDNA and genomic clones containing the polynucleotide sequence set forth in the Sequence Listing. Such hybridization techniques are well known to the skilled artisan. Preferred stringent hybridization conditions include overnight incubation at 42°C in a solution comprising: 50% formamide, 5xSSC (150mM NaCl, 15mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10 % dextran sulfate, and 20 microgram/ml denatured, sheared salmon sperm DNA; followed by washing the filters in 0.1x SSC at about 65°C. Thus the present invention also includes isolated polynucleotides, preferably with a nucleotide sequence of at least 100, obtained by screening a library under stringent hybridization conditions with a labeled probe having the sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides.

The skilled artisan will appreciate that, in many cases, an isolated cDNA sequence will be incomplete, in that the region coding for the polypeptide does not extend all the way through to the 5' terminus. This is a consequence of reverse transcriptase, an enzyme with inherently low "processivity" (a measure of the ability of the enzyme to remain attached to the template during the polymerisation reaction), failing to complete a DNA copy of the mRNA template during first strand cDNA synthesis.

There are several methods available and well known to those skilled in the art to obtain full-length cDNAs, or extend short cDNAs, for example those based on the method of Rapid Amplification of cDNA ends (RACE) (see, for example, Frohman et al., Proc Nat Acad Sci USA 85, 8998-9002, 1988). Recent modifications of the technique, exemplified by the Marathon (trade mark) technology (Clontech Laboratories Inc.) for example, have significantly simplified the search for longer cDNAs. In the Marathon (trade mark) technology, cDNAs have been prepared from mRNA extracted from a chosen tissue and an 'adaptor' sequence ligated onto each end. Nucleic acid amplification (PCR) is then carried out to amplify the "missing" 5' end of the cDNA using a combination of gene specific and adaptor specific oligonucleotide primers. The PCR reaction is then repeated using 'nested' primers, that is, primers designed to anneal within the amplified product (typically an adapter specific primer that anneals further 3' in the adaptor sequence and a gene specific

primer that anneals further 5' in the known gene sequence). The products of this reaction can then be analyzed by DNA sequencing and a full-length cDNA constructed either by joining the product directly to the existing cDNA to give a complete sequence, or carrying out a separate full-length PCR using the new sequence information for the design of the 5' primer.

Recombinant polypeptides of the present invention may be prepared by processes well known in the art from genetically engineered host cells comprising expression systems. Accordingly, in a further aspect, the present invention relates to expression systems comprising a polynucleotide or polynucleotides of the present invention, to host cells which are genetically engineered with such expression systems and to the production of polypeptides of the invention by recombinant techniques. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention.

For recombinant production, host cells can be genetically engineered to incorporate expression systems or portions thereof for polynucleotides of the present invention. Polynucleotides may be introduced into host cells by methods described in many standard laboratory manuals, such as Davis et al., Basic Methods in Molecular Biology (1986) and Sambrook *et al.*(*ibid*). Preferred methods of introducing polynucleotides into host cells include, for instance, calcium phosphate transfection, DEAE-dextran mediated transfection, transvection, micro-injection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction or infection.

Representative examples of appropriate hosts include bacterial cells, such as *Streptococci*, *Staphylococci*, *E. coli*, *Streptomyces* and *Bacillus subtilis* cells; fungal cells, such as yeast cells and *Aspergillus* cells; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, HEK 293 and Bowes melanoma cells; and plant cells.

A great variety of expression systems can be used, for instance, chromosomal, episomal and virus-derived systems, *e.g.*, vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations thereof, such as those derived from plasmid and bacteriophage genetic elements, such as cosmids and phagemids. The expression systems may contain control regions that regulate as well as engender expression. Generally, any system or vector that is able to maintain, propagate or express a polynucleotide to produce a

polypeptide in a host may be used. The appropriate polynucleotide sequence may be inserted into an expression system by any of a variety of well-known and routine techniques, such as, for example, those set forth in Sambrook *et al.*, (*ibid*). Appropriate secretion signals may be incorporated into the desired polypeptide to allow secretion of the translated protein into the lumen of the endoplasmic reticulum, the periplasmic space or the extracellular environment. These signals may be endogenous to the polypeptide or they may be heterologous signals.

If a polypeptide of the present invention is to be expressed for use in screening assays, it is generally preferred that the polypeptide be produced at the surface of the cell. In this event, the cells may be harvested prior to use in the screening assay. If the polypeptide is secreted into the medium, the medium can be recovered in order to recover and purify the polypeptide. If produced intracellularly, the cells must first be lysed before the polypeptide is recovered.

Polypeptides of the present invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography is employed for purification. Well known techniques for refolding proteins may be employed to regenerate active conformation when the polypeptide is denatured during intracellular synthesis, isolation and/or purification.

Polynucleotides of the present invention may be used as diagnostic reagents, through detecting mutations in the associated gene. Detection of a mutated form of a gene is characterized by the polynucleotides set forth in the Sequence Listing in the cDNA or genomic sequence and which is associated with a dysfunction. Will provide a diagnostic tool that can add to, or define, a diagnosis of a disease, or susceptibility to a disease, which results from under-expression, over-expression or altered spatial or temporal expression of the gene. Individuals carrying mutations in the gene may be detected at the DNA level by a variety of techniques well known in the art.

Nucleic acids for diagnosis may be obtained from a subject's cells, such as from blood, urine, saliva, tissue biopsy or autopsy material. The genomic DNA may be used directly for detection or it may be amplified enzymatically by using PCR, preferably RT-PCR, or other amplification techniques prior to analysis. RNA or cDNA may also be used in similar fashion. Deletions and insertions can be detected by a change in size of the amplified product in comparison to the normal genotype. Point mutations can be identified

by hybridizing amplified DNA to labeled nucleotide sequences of the genes set forth in Table I. Perfectly matched sequences can be distinguished from mismatched duplexes by RNase digestion or by differences in melting temperatures. DNA sequence difference may also be detected by alterations in the electrophoretic mobility of DNA fragments in gels, with or without denaturing agents, or by direct DNA sequencing (see, for instance, Myers *et al.*, Science (1985) 230:1242). Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and S1 protection or the chemical cleavage method (see Cotton *et al.*, Proc Natl Acad Sci USA (1985) 85: 4397-4401).

An array of oligonucleotides probes comprising polynucleotide sequences or fragments thereof of the genes set forth in Table I can be constructed to conduct efficient screening of *e.g.*, genetic mutations. Such arrays are preferably high density arrays or grids. Array technology methods are well known and have general applicability and can be used to address a variety of questions in molecular genetics including gene expression, genetic linkage, and genetic variability, see, for example, M. Chee et al., Science, 274, 610-613 (1996) and other references cited therein.

Detection of abnormally decreased or increased levels of polypeptide or mRNA expression may also be used for diagnosing or determining susceptibility of a subject to a disease of the invention. Decreased or increased expression can be measured at the RNA level using any of the methods well known in the art for the quantitation of polynucleotides, such as, for example, nucleic acid amplification, for instance PCR, RT-PCR, RNase protection, Northern blotting and other hybridization methods. Assay techniques that can be used to determine levels of a protein, such as a polypeptide of the present invention, in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radio-immunoassays, competitive-binding assays, Western Blot analysis and ELISA assays.

Thus in another aspect, the present invention relates to a diagnostic kit comprising:
(a) a polynucleotide of the present invention, preferably the nucleotide sequence set forth in the Sequence Listing , or a fragment or an RNA transcript thereof;
(b) a nucleotide sequence complementary to that of (a);
(c) a polypeptide of the present invention, preferably the polypeptide set forth in the Sequence Listing or a fragment thereof; or
(d) an antibody to a polypeptide of the present invention, preferably to the polypeptide set forth in the Sequence Listing .

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component. Such a kit will be of use in diagnosing a disease or susceptibility to a disease, particularly diseases of the invention, amongst others.

The polynucleotide sequences of the present invention are valuable for chromosome localisation studies. The sequences set forth in the Sequence Listing are specifically targeted to, and can hybridize with, a particular location on an individual human chromosome. The mapping of relevant sequences to chromosomes according to the present invention is an important first step in correlating those sequences with gene associated disease. Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found in, for example, V. McKusick, Mendelian Inheritance in Man (available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and diseases that have been mapped to the same chromosomal region are then identified through linkage analysis (co-inheritance of physically adjacent genes). Precise human chromosomal localisations for a genomic sequence (gene fragment etc.) can be determined using Radiation Hybrid (RH) Mapping (Walter, M. Spillett, D., Thomas, P., Weissenbach, J., and Goodfellow, P., (1994) A method for constructing radiation hybrid maps of whole genomes, Nature Genetics 7, 22-28). A number of RH panels are available from Research Genetics (Huntsville, AL, USA) e.g. the GeneBridge4 RH panel (Hum Mol Genet 1996 Mar;5(3):339-46 A radiation hybrid map of the human genome. Gyapay G, Schmitt K, Fizames C, Jones H, Vega-Czarny N, Spillett D, Muselet D, Prud'Homme JF, Dib C, Auffray C, Morissette J, Weissenbach J, Goodfellow PN). To determine the chromosomal location of a gene using this panel, 93 PCRs are performed using primers designed from the gene of interest on RH DNAs. Each of these DNAs contains random human genomic fragments maintained in a hamster background (human / hamster hybrid cell lines). These PCRs result in 93 scores indicating the presence or absence of the PCR product of the gene of interest. These scores are compared with scores created using PCR products from genomic sequences of known location. This comparison is conducted at http://www.genome.wi.mit.edu/.

The polynucleotide sequences of the present invention are also valuable tools for tissue expression studies. Such studies allow the determination of expression patterns of polynucleotides of the present invention which may give an indication as to the expression patterns of the encoded polypeptides in tissues, by detecting the mRNAs that encode them. The techniques used are well known in the art and include in situ hydridization techniques to clones arrayed on a grid, such as cDNA microarray hybridization (Schena *et al*, Science, 270, 467-470, 1995 and Shalon *et al*, Genome Res, 6, 639-645, 1996) and nucleotide amplification techniques such as PCR. A preferred method uses the TAQMAN (Trade mark) technology available from Perkin Elmer. Results from these studies can provide an

indication of the normal function of the polypeptide in the organism. In addition, comparative studies of the normal expression pattern of mRNAs with that of mRNAs encoded by an alternative form of the same gene (for example, one having an alteration in polypeptide coding potential or a regulatory mutation) can provide valuable insights into the role of the polypeptides of the present invention, or that of inappropriate expression thereof in disease. Such inappropriate expression may be of a temporal, spatial or simply quantitative nature.

A further aspect of the present invention relates to antibodies. The polypeptides of the invention or their fragments, or cells expressing them, can be used as immunogens to produce antibodies that are immunospecific for polypeptides of the present invention. The term "immunospecific" means that the antibodies have substantially greater affinity for the polypeptides of the invention than their affinity for other related polypeptides in the prior art.

Antibodies generated against polypeptides of the present invention may be obtained by administering the polypeptides or epitope-bearing fragments, or cells to an animal, preferably a non-human animal, using routine protocols. For preparation of monoclonal antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler, G. and Milstein, C., Nature (1975) 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor *et al.*, Immunology Today (1983) 4:72) and the EBV-hybridoma technique (Cole *et al.*, Monoclonal Antibodies and Cancer Therapy, 77-96, Alan R. Liss, Inc., 1985).

Techniques for the production of single chain antibodies, such as those described in U.S. Patent No. 4,946,778, can also be adapted to produce single chain antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms, including other mammals, may be used to express humanized antibodies.

The above-described antibodies may be employed to isolate or to identify clones expressing the polypeptide or to purify the polypeptides by affinity chromatography. Antibodies against polypeptides of the present invention may also be employed to treat diseases of the invention, amongst others.

Polypeptides and polynucleotides of the present invention may also be used as vaccines. Accordingly, in a further aspect, the present invention relates to a method for inducing an immunological response in a mammal that comprises inoculating the mammal with a polypeptide of the present invention, adequate to produce antibody and/or T cell immune response, including, for example, cytokine-producing T cells or cytotoxic T cells,

to protect said animal from disease, whether that disease is already established within the individual or not. An immunological response in a mammal may also be induced by a method comprises delivering a polypeptide of the present invention *via* a vector directing expression of the polynucleotide and coding for the polypeptide *in vivo* in order to induce such an immunological response to produce antibody to protect said animal from diseases of the invention. One way of administering the vector is by accelerating it into the desired cells as a coating on particles or otherwise. Such nucleic acid vector may comprise DNA, RNA, a modified nucleic acid, or a DNA/RNA hybrid. For use a vaccine, a polypeptide or a nucleic acid vector will be normally provided as a vaccine formulation (composition). The formulation may further comprise a suitable carrier. Since a polypeptide may be broken down in the stomach, it is preferably administered parenterally (for instance, subcutaneous, intra-muscular, intravenous, or intra-dermal injection). Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions that may contain anti-oxidants, buffers, bacteriostats and solutes that render the formulation instonic with the blood of the recipient; and aqueous and non-aqueous sterile suspensions that may include suspending agents or thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example, sealed ampoules and vials and may be stored in a freeze-dried condition requiring only the addition of the sterile liquid carrier immediately prior to use. The vaccine formulation may also include adjuvant systems for enhancing the immunogenicity of the formulation, such as oil-in water systems and other systems known in the art. The dosage will depend on the specific activity of the vaccine and can be readily determined by routine experimentation.

Polypeptides of the present invention have one or more biological functions that are of relevance in one or more disease states, in particular the diseases of the invention hereinbefore mentioned. It is therefore useful to identify compounds that stimulate or inhibit the function or level of the polypeptide. Accordingly, in a further aspect, the present invention provides for a method of screening compounds to identify those that stimulate or inhibit the function or level of the polypeptide. Such methods identify agonists or antagonists that may be employed for therapeutic and prophylactic purposes for such diseases of the invention as hereinbefore mentioned. Compounds may be identified from a variety of sources, for example, cells, cell-free preparations, chemical libraries, collections of chemical compounds, and natural product mixtures. Such agonists or antagonists so-identified may be natural or modified substrates, ligands, receptors, enzymes, etc., as the case may be, of the polypeptide; a structural or functional mimetic thereof (see Coligan *et al.*, Current Protocols in Immunology 1(2):Chapter 5 (1991)) or a small molecule. Such

small molecules preferably have a molecular weight below 2,000 daltons, more preferably between 300 and 1,000 daltons, and most preferably between 400 and 700 daltons. It is preferred that these small molecules are organic molecules.

The screening method may simply measure the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide, or a fusion protein thereof, by means of a label directly or indirectly associated with the candidate compound. Alternatively, the screening method may involve measuring or detecting (qualitatively or quantitatively) the competitive binding of a candidate compound to the polypeptide against a labeled competitor (*e.g.* agonist or antagonist). Further, these screening methods may test whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells bearing the polypeptide. Inhibitors of activation are generally assayed in the presence of a known agonist and the effect on activation by the agonist by the presence of the candidate compound is observed. Further, the screening methods may simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide of the present invention, to form a mixture, measuring an activity of the genes set forth in Table I in the mixture, and comparing activity of the mixture of the genes set forth in Table I to a control mixture which contains no candidate compound.

Polypeptides of the present invention may be employed in conventional low capacity screening methods and also in high-throughput screening (HTS) formats. Such HTS formats include not only the well-established use of 96- and, more recently, 384-well micotiter plates but also emerging methods such as the nanowell method described by Schullek et al, Anal Biochem., 246, 20-29, (1997).

Fusion proteins, such as those made from Fc portion and polypeptide of the genes set forth in Table I, as hereinbefore described, can also be used for high-throughput screening assays to identify antagonists for the polypeptide of the present invention (see D. Bennett *et al.*, J Mol Recognition, 8:52-58 (1995); and K. Johanson *et al.*, J Biol Chem, 270(16):9459-9471 (1995)).

The polynucleotides, polypeptides and antibodies to the polypeptide of the present invention may also be used to configure screening methods for detecting the effect of added compounds on the production of mRNA and polypeptide in cells. For example, an ELISA assay may be constructed for measuring secreted or cell associated levels of polypeptide using monoclonal and polyclonal antibodies by standard methods known in the art. This can be used to discover agents that may inhibit or enhance the production of polypeptide (also called antagonist or agonist, respectively) from suitably manipulated cells or tissues.

A polypeptide of the present invention may be used to identify membrane bound or soluble receptors, if any, through standard receptor binding techniques known in the art. These include, but are not limited to, ligand binding and crosslinking assays in which the polypeptide is labeled with a radioactive isotope (for instance, ^{125}I), chemically modified (for instance, biotinylated), or fused to a peptide sequence suitable for detection or purification, and incubated with a source of the putative receptor (cells, cell membranes, cell supernatants, tissue extracts, bodily fluids). Other methods include biophysical techniques such as surface plasmon resonance and spectroscopy. These screening methods may also be used to identify agonists and antagonists of the polypeptide that compete with the binding of the polypeptide to its receptors, if any. Standard methods for conducting such assays are well understood in the art.

Examples of antagonists of polypeptides of the present invention include antibodies or, in some cases, oligonucleotides or proteins that are closely related to the ligands, substrates, receptors, enzymes, etc., as the case may be, of the polypeptide, *e.g.*, a fragment of the ligands, substrates, receptors, enzymes, etc.; or a small molecule that bind to the polypeptide of the present invention but do not elicit a response, so that the activity of the polypeptide is prevented.

Screening methods may also involve the use of transgenic technology and the genes set forth in Table I. The art of constructing transgenic animals is well established. For example, the genes set forth in Table I may be introduced through microinjection into the male pronucleus of fertilized oocytes, retroviral transfer into pre- or post-implantation embryos, or injection of genetically modified, such as by electroporation, embryonic stem cells into host blastocysts. Particularly useful transgenic animals are so-called "knock-in" animals in which an animal gene is replaced by the human equivalent within the genome of that animal. Knock-in transgenic animals are useful in the drug discovery process, for target validation, where the compound is specific for the human target. Other useful transgenic animals are so-called "knock-out" animals in which the expression of the animal ortholog of a polypeptide of the present invention and encoded by an endogenous DNA sequence in a cell is partially or completely annulled. The gene knock-out may be targeted to specific cells or tissues, may occur only in certain cells or tissues as a consequence of the limitations of the technology, or may occur in all, or substantially all, cells in the animal. Transgenic animal technology also offers a whole animal expression-cloning system in which introduced genes are expressed to give large amounts of polypeptides of the present invention

Screening kits for use in the above described methods form a further aspect of the present invention. Such screening kits comprise:

(a) a polypeptide of the present invention;

(b) a recombinant cell expressing a polypeptide of the present invention;

(c) a cell membrane expressing a polypeptide of the present invention; or

(d) an antibody to a polypeptide of the present invention;

which polypeptide is preferably that set forth in the Sequence Listing.

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component.

Glossary

The following definitions are provided to facilitate understanding of certain terms used frequently hereinbefore.

"Antibodies" as used herein includes polyclonal and monoclonal antibodies, chimeric, single chain, and humanized antibodies, as well as Fab fragments, including the products of an

Fab or other immunoglobulin expression library.

"Isolated" means altered "by the hand of man" from its natural state, *i.e.*, if it occurs in nature, it has been changed or removed from its original environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living organism is not "isolated," but the same polynucleotide or polypeptide separated from the coexisting materials of its natural state is "isolated", as the term is employed herein. Moreover, a polynucleotide or polypeptide that is introduced into an organism by transformation, genetic manipulation or by any other recombinant method is "isolated" even if it is still present in said organism, which organism may be living or non-living.

"Secreted protein activity or secreted polypeptide activity" or "biological activity of the secreted protein or secreted polypeptide" refers to the metabolic or physiologic function of said secreted protein including similar activities or improved activities or these activities with decreased undesirable side-effects. Also included are antigenic and immunogenic activities of said secreted protein.

"Secreted protein gene" refers to a polynucleotide comprising any of the attached nucleotide sequences or allelic variants thereof and/or their complements.

"Polynucleotide" generally refers to any polyribonucleotide (RNA) or polydeoxribonucleotide (DNA), which may be unmodified or modified RNA or DNA. "Polynucleotides" include, without limitation, single- and double-stranded DNA, DNA that

is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, "polynucleotide" refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The term "polynucleotide" also includes DNAs or RNAs containing one or more modified bases and DNAs or RNAs with backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications may be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically or metabolically modified forms of polynucleotides as typically found in nature, as well as the chemical forms of DNA and RNA characteristic of viruses and cells. "Polynucleotide" also embraces relatively short polynucleotides, often referred to as oligonucleotides.

"Polypeptide" refers to any polypeptide comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres. "Polypeptide" refers to both short chains, commonly referred to as peptides, oligopeptides or oligomers, and to longer chains, generally referred to as proteins. Polypeptides may contain amino acids other than the 20 gene-encoded amino acids. "Polypeptides" include amino acid sequences modified either by natural processes, such as post-translational processing, or by chemical modification techniques that are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications may occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present to the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched and branched cyclic polypeptides may result from post-translation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, biotinylation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation,

myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination (see, for instance, Proteins - Structure and Molecular Properties, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York, 1993; Wold, F., Post-translational Protein Modifications: Perspectives and Prospects, 1-12, in Post-translational Covalent Modification of Proteins, B. C. Johnson, Ed., Academic Press, New York, 1983; Seifter *et al.*, "Analysis for protein modifications and nonprotein cofactors", Meth Enzymol, 182, 626-646, 1990, and Rattan *et al.*, "Protein Synthesis: Post-translational Modifications and Aging", Ann NY Acad Sci, 663, 48-62, 1992).

"Fragment" of a polypeptide sequence refers to a polypeptide sequence that is shorter than the reference sequence but that retains essentially the same biological function or activity as the reference polypeptide. "Fragment" of a polynucleotide sequence refers to a polynucleotide sequence that is shorter than the reference sequence set forth in the Sequence Listing.

"Variant" refers to a polynucleotide or polypeptide that differs from a reference polynucleotide or polypeptide, but retains the essential properties thereof. A typical variant of a polynucleotide differs in nucleotide sequence from the reference polynucleotide. Changes in the nucleotide sequence of the variant may or may not alter the amino acid sequence of a polypeptide encoded by the reference polynucleotide. Nucleotide changes may result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference sequence, as discussed below. A typical variant of a polypeptide differs in amino acid sequence from the reference polypeptide. Generally, alterations are limited so that the sequences of the reference polypeptide and the variant are closely similar overall and, in many regions, identical. A variant and reference polypeptide may differ in amino acid sequence by one or more substitutions, insertions, deletions in any combination. A substituted or inserted amino acid residue may or may not be one encoded by the genetic code. Typical conservative substitutions include Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe and Tyr. A variant of a polynucleotide or polypeptide may be naturally occurring such as an allele, or it may be a variant that is not known to occur naturally. Non-naturally occurring variants of polynucleotides and polypeptides may be made by mutagenesis techniques or by direct synthesis. Also included as variants are polypeptides having one or more post-translational modifications, for instance glycosylation, phosphorylation, methylation, ADP ribosylation and the like. Embodiments include methylation of the N-terminal amino acid, phosphorylations of serines and threonines and modification of C-terminal glycines.

"Allele" refers to one of two or more alternative forms of a gene occurring at a given locus in the genome.

"Polymorphism" refers to a variation in nucleotide sequence (and encoded polypeptide sequence, if relevant) at a given position in the genome within a population.

"Single Nucleotide Polymorphism" (SNP) refers to the occurrence of nucleotide variability at a single nucleotide position in the genome, within a population. An SNP may occur within a gene or within intergenic regions of the genome. SNPs can be assayed using Allele Specific Amplification (ASA). For the process at least 3 primers are required. A common primer is used in reverse complement to the polymorphism being assayed. This common primer can be between 50 and 1500 bps from the polymorphic base. The other two (or more) primers are identical to each other except that the final 3' base wobbles to match one of the two (or more) alleles that make up the polymorphism. Two (or more) PCR reactions are then conducted on sample DNA, each using the common primer and one of the Allele Specific Primers.

"Splice Variant" as used herein refers to cDNA molecules produced from RNA molecules initially transcribed from the same genomic DNA sequence but which have undergone alternative RNA splicing. Alternative RNA splicing occurs when a primary RNA transcript undergoes splicing, generally for the removal of introns, which results in the production of more than one mRNA molecule each of that may encode different amino acid sequences. The term splice variant also refers to the proteins encoded by the above cDNA molecules.

"Identity" reflects a relationship between two or more polypeptide sequences or two or more polynucleotide sequences, determined by comparing the sequences. In general, identity refers to an exact nucleotide to nucleotide or amino acid to amino acid correspondence of the two polynucleotide or two polypeptide sequences, respectively, over the length of the sequences being compared.

"% Identity" - For sequences where there is not an exact correspondence, a "% identity" may be determined. In general, the two sequences to be compared are aligned to give a maximum correlation between the sequences. This may include inserting "gaps" in either one or both sequences, to enhance the degree of alignment. A % identity may be determined over the whole length of each of the sequences being compared (so-called global alignment), that is particularly suitable for sequences of the same or very similar length, or over shorter, defined lengths (so-called local alignment), that is more suitable for sequences of unequal length.

"Similarity" is a further, more sophisticated measure of the relationship between two polypeptide sequences. In general, "similarity" means a comparison between the amino acids of two polypeptide chains, on a residue by residue basis, taking into account not only exact correspondences between a between pairs of residues, one from each of the sequences being compared (as for identity) but also, where there is not an exact correspondence, whether, on an evolutionary basis, one residue is a likely substitute for the other. This likelihood has an associated "score" from which the "% similarity" of the two sequences can then be determined.

Methods for comparing the identity and similarity of two or more sequences are well known in the art. Thus for instance, programs available in the Wisconsin Sequence Analysis Package, version 9.1 (Devereux J et al, Nucleic Acids Res, 12, 387-395, 1984, available from Genetics Computer Group, Madison, Wisconsin, USA), for example the programs BESTFIT and GAP, may be used to determine the % identity between two polynucleotides and the % identity and the % similarity between two polypeptide sequences. BESTFIT uses the "local homology" algorithm of Smith and Waterman (J Mol Biol, 147,195-197, 1981, Advances in Applied Mathematics, 2, 482-489, 1981) and finds the best single region of similarity between two sequences. BESTFIT is more suited to comparing two polynucleotide or two polypeptide sequences that are dissimilar in length, the program assuming that the shorter sequence represents a portion of the longer. In comparison, GAP aligns two sequences, finding a "maximum similarity", according to the algorithm of Neddleman and Wunsch (J Mol Biol, 48, 443-453, 1970). GAP is more suited to comparing sequences that are approximately the same length and an alignment is expected over the entire length. Preferably, the parameters "Gap Weight" and "Length Weight" used in each program are 50 and 3, for polynucleotide sequences and 12 and 4 for polypeptide sequences, respectively. Preferably, % identities and similarities are determined when the two sequences being compared are optimally aligned.

Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul S F et al, J Mol Biol, 215, 403-410, 1990, Altschul S F et al, Nucleic Acids Res., 25:389-3402, 1997, available from the National Center for Biotechnology Information (NCBI), Bethesda, Maryland, USA and accessible through the home page of the NCBI at www.ncbi.nlm.nih.gov) and FASTA (Pearson W R, Methods in Enzymology, 183, 63-99, 1990; Pearson W R and Lipman D J, Proc Nat Acad Sci USA, 85, 2444-2448,1988, available as part of the Wisconsin Sequence Analysis Package).

Preferably, the BLOSUM62 amino acid substitution matrix (Henikoff S and Henikoff J G, Proc. Nat. Acad Sci. USA, 89, 10915-10919, 1992) is used in polypeptide sequence comparisons including where nucleotide sequences are first translated into amino acid sequences before comparison.

Preferably, the program BESTFIT is used to determine the % identity of a query polynucleotide or a polypeptide sequence with respect to a reference polynucleotide or a polypeptide sequence, the query and the reference sequence being optimally aligned and the parameters of the program set at the default value, as hereinbefore described.

"Identity Index" is a measure of sequence relatedness which may be used to compare a candidate sequence (polynucleotide or polypeptide) and a reference sequence. Thus, for instance, a candidate polynucleotide sequence having, for example, an Identity Index of 0.95 compared to a reference polynucleotide sequence is identical to the reference sequence except that the candidate polynucleotide sequence may include on average up to five differences per each 100 nucleotides of the reference sequence. Such differences are selected from the group consisting of at least one nucleotide deletion, substitution, including transition and transversion, or insertion. These differences may occur at the 5' or 3' terminal positions of the reference polynucleotide sequence or anywhere between these terminal positions, interspersed either individually among the nucleotides in the reference sequence or in one or more contiguous groups within the reference sequence. In other words, to obtain a polynucleotide sequence having an Identity Index of 0.95 compared to a reference polynucleotide sequence, an average of up to 5 in every 100 of the nucleotides of the in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

Similarly, for a polypeptide, a candidate polypeptide sequence having, for example, an Identity Index of 0.95 compared to a reference polypeptide sequence is identical to the reference sequence except that the polypeptide sequence may include an average of up to five differences per each 100 amino acids of the reference sequence. Such differences are selected from the group consisting of at least one amino acid deletion, substitution, including conservative and non-conservative substitution, or insertion. These differences may occur at the amino- or carboxy-terminal positions of the reference polypeptide sequence or anywhere between these terminal positions, interspersed either individually among the amino acids in the reference sequence or in one or more contiguous groups within the reference sequence. In other words, to obtain a polypeptide sequence having an Identity Index of 0.95 compared to a reference polypeptide sequence, an average of up to 5

in every 100 of the amino acids in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

The relationship between the number of nucleotide or amino acid differences and the Identity Index may be expressed in the following equation:

$$n_a \leq x_a - (x_a \bullet I),$$

in which:

n_a is the number of nucleotide or amino acid differences,

x_a is the total number of nucleotides or amino acids in a sequence set forth in the Sequence Listing,

I is the Identity Index,

• is the symbol for the multiplication operator, and

in which any non-integer product of x_a and I is rounded down to the nearest integer prior to subtracting it from x_a.

"Homolog" is a generic term used in the art to indicate a polynucleotide or polypeptide sequence possessing a high degree of sequence relatedness to a reference sequence. Such relatedness may be quantified by determining the degree of identity and/or similarity between the two sequences as hereinbefore defined. Falling within this generic term are the terms "ortholog", and "paralog". "Ortholog" refers to a polynucleotide or polypeptide that is the functional equivalent of the polynucleotide or polypeptide in another species. "Paralog" refers to a polynucleotideor polypeptide that within the same species which is functionally similar.

"Fusion protein" refers to a protein encoded by two, often unrelated, fused genes or fragments thereof. In one example, EP-A-0 464 533-A discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, employing an immunoglobulin Fc region as a part of a fusion protein is advantageous for use in therapy and diagnosis resulting in, for example, improved pharmacokinetic properties [see, *e.g.*, EP-A 0232 262]. On the other hand, for some uses it would be desirable to be able to delete the Fc part after the fusion protein has been expressed, detected and purified.

All publications and references, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference in their entirety as if each individual publication or reference were specifically and individually indicated to be incorporated by reference herein as being fully set forth. Any patent application to which

this application claims priority is also incorporated by reference herein in its entirety in the manner described above for publications and references.

Table I.

Gene Name	GSK Gene ID	Nucleic Acid SEQ ID NO's	Corresponding Protein SEQ ID NO's
sbg237163LIPASE	237163	SEQ ID NO:1	SEQ ID NO:23
sbg251170CEAa	251170	SEQ ID NO:2 SEQ ID NO:3	SEQ ID NO:24 SEQ ID NO:25
sbg389686WNT15a	389686	SEQ ID NO:4 SEQ ID NO:5	SEQ ID NO:26 SEQ ID NO:27
sbg236015LIPASE	236015	SEQ ID NO:6 SEQ ID NO:7	SEQ ID NO:28 SEQ ID NO:29
sbg417005LAMININ_ALPHA	417005	SEQ ID NO:8 SEQ ID NO:9	SEQ ID NO:30 SEQ ID NO:31
sbg425649KINASEa	425649	SEQ ID NO:10	SEQ ID NO:32
sbg419582PROTOCADHERIN	419582	SEQ ID NO:11 SEQ ID NO:12	SEQ ID NO:33 SEQ ID NO:34
sbg453915TECTORINa	453915	SEQ ID NO:13	SEQ ID NO:35
SBh385630.antiinflam	385630	SEQ ID NO:14 SEQ ID NO:15	SEQ ID NO:36 SEQ ID NO:37
sbg471005nAChR	471005	SEQ ID NO:16	SEQ ID NO:38
sbg442445PROa	442445	SEQ ID NO:17	SEQ ID NO:39
sbg456548CytoRa	456548	SEQ ID NO:18 SEQ ID NO:19	SEQ ID NO:40 SEQ ID NO:41
sbg456548CytoRa	456548b	SEQ ID NO:20	SEQ ID NO:42
sbg442358PROa	442358	SEQ ID NO:21 SEQ ID NO:22	SEQ ID NO:43 SEQ ID NO:44

Table II

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg237163 LIPASE	Pancreatic lipase	GB:AC011328 Direct submitted (06-OCT-1999) Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02453, USA	Mouse pancreatic lipase related protein 1, gi: 9256628 Remington,S.G., Lima,P.H. and Nelson,J.D. Invest. Ophthalmol. Vis. Sci. 40 (6), 1081-1090 (1999)	Secreted
sbg251170C EAa	Carcinoembryonic antigen	GB:AC020914 Submitted (12-JAN-2000) Production Sequencing Facility, DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA	Mouse putative protein, gi:12842545 Carninci,P., Shibata,Y., Hayatsu,N., Sugahara,Y., Shibata,K., Itoh,M., Konno,H., Okazaki,Y., Muramatsu,M. and Hayashizaki,Y. Genome Res. 10 (10), 1617-1630 (2000).	Secreted
sbg389686 WNT15a	WNT15	GB:AC015855 Directly submitted (17-NOV-1999) Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Chicken WNT14 protein, gi:3915306 Bergstein I, Eisenberg LM, Bhalerao J, Jenkins NA, Copeland NG, Osborne MP, Bowcock AM, Brown AM; 1997; Genomics 46:450-8.	Secreted
sbg236015L IPASE	Lysosomal acid lipase	GB:AL358532 Directly submitted (15-DEC-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Rat lingual lipase, gi:126307 Docherty,A.J., Bodmer,M.W., Angal,S., Verger,R., Riviere,C., Lowe,P.A., Lyons,A., Emtage,J.S. and Harris,T.J. Nucleic Acids Res. 13 (6), 1891-1903 (1985)	Secreted
sbg417005L AMININ_ALPHA	Laminin alpha	GB:AL354836 Direct submitted (02-MAY-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA	Human laminin alpha 5, gi:12274842 Submitted (14-FEB-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Secreted
sbg425649K INASEa	Casein kinase I-alpha	GB:AL356107 Submitted (16-MAY-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human casein kinase I-alpha, gi:2134872 Fish,K.J., Cegielska,A., Getman,M.E., Landes,G.M. and Virshup,D.M. J. Biol. Chem. 270 (25), 14875-14883 (1995)	Cytosolic

sbg419582PROTOCADHERIN	Protocadherin	GB:AL355593 Direct submitted (17-MAY-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human protocadherin 68 gi:11433373 Submitted (16-NOV-2000) by National Center for Biotechnology Information, NIH, Bethesda, MD 20894, USA	Secreted
sbg453915TECTORINa	Tectorin Beta	SC:AL157786 Submitted (04-MAY-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Mouse tectorin beta, gi:7363457 Legan,P.K., Rau,A., Keen,J.N. and Richardson,G.P. J. Biol. Chem. 272 (13), 8791-8801 (1997)	Secreted
SBh385630.antiinflam	Lipase	GB:AC015525 Submitted (16-NOV-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Rabbit lacrimal lipase, gi:13560884 Submitted (20-FEB-2001) Ophthalmology, Regions Hospital, 640 Jackson Street, St. Paul, MN 55101, USA	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg47100 5nAChR	Nicotinic acetylcholine receptor	GB:AC060812 Direct submitted (20-APR-2000) Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human cholinergic receptor, nicotinic, alpha polypeptide 10, gi:11138123 Lustig,L.R., Peng,H., Hiel,H., Yamamoto,T. and Fuchs,P.A. Genomics 73 (3), 272-283 (2001)	Membrane-bound
sbg44244 5PROa	Leucine rich repeat protein	GB:AC060234 Submitted (20-APR-2000) Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02453, USA	RIKEN cDNA mouse 4930442L21 gene Carninci,P., Shibata,Y., Hayatsu,N., Sugahara,Y., Shibata,K., Itoh,M., Konno,H., Okazaki,Y., Muramatsu,M. and Hayashizaki,Y. Genome Res. 10 (10), 1617-1630 (2000)	Cytosolic
sbg45654 8CytoRa	Cytokine receptor	GB:AL158138 Submitted (20-JAN-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human IL20 receptor, gi:7657691 Xie MH, Aggarwal S, Ho WH, Foster J, Zhang Z, Stinson J, Wood WI, Goddard AD and Gurney AL. J. Biol. Chem. 275 (40), 31335-31339 (2000)	Membrane-bound
sbg44235 8PROa	Leucine rich repeat protein	GB:AL139099 Submitted (23-MAY-2000) by Genoscope - Centre National de Sequencage : BP 191 91006 EVRY cedex - FRANCE	Human EXMAD-9 geneseqp: AAB27231 Submitted by INCYTE GENOMICS INC Application and publication date: WO200068380-A2, 16-NOV-00	Membrane-bound

Table III

Gene Name	Uses	Associated Diseases
sbg237163 LIPASE	An embodiment of the invention is the use of sbg237163 LIPASE as replacement enzymes for patients with chronic pancreatitis. A close homologue of sbg237163 LIPASE is pancreatic lipase. Pancreatic lipase hydrolyzes dietary long chain triacylglycerol to free fatty acids and monoacylglycerols in the intestinal lumen (Lowe ME, Rosenblum JL, and Strauss AW; 1989; J Biol Chem 264:20042-8). Pancreatic steatorrhea and pancreatic diabetes are the dominant symptoms of patients in a certain stage of chronic pancreatitis. In this stage, the nutritional state is greatly disturbed and hypoglycemia and labile infection are involved. Pancreatic enzyme replacement therapy is the principal treatment method for pancreatic steatorrhea (Nakamura T, Takeuchi T, and Tando Y; 1998; Pancreas 16:329-36.	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation.
sbg251170CEAa	An embodiment of the invention is the use of sbg251170CEAa as cell-surface molecules mediating cell-specific interactions in normal and neoplastic cells. A close homologue of sbg251170CEAa is carcinoembryonic antigen-related cell adhesion molecule 6. Carcinoembryonic antigen-related cell adhesion molecule 6 is claimed to function as a cell-surface molecules mediating cell-specific interactions in normal and neoplastic cells (1. Barnett T, Goebel SJ, Nothdurft MA, Elting JJ, Carcinoembryonic antigen family: characterization of cDNAs coding for NCA and CEA and suggestion of nonrandom sequence variation in their conserved loop-domains. Genomics 1988 Jul;3(1):59-66. 2. Inazawa J, Abe T, Inoue K, Misawa S, Oikawa S, Nakazato H, Yoshida MC. Regional assignment of nonspecific cross-reacting antigen (NCA) of the CEA gene family to chromosome 19 at band q13.2. Cytogenet Cell Genet 1989;52(1-2):28-31).	Cancer, autoimmune disorders, wound healing disorders, hematopoietic disorders and infection
sbg389686 WNT15a	An embodiment of the invention is the use of sbg389686WNT15a in regulation of cell growth and differentiation. Close homologues of sbg389686WNT15a are Wnt proteins. Wnt proteins are involved in critical developmental processes in both vertebrates and invertebrates and are implicated in regulation of cell growth and differentiation in certain adult mammalian tissues (Bergstein I, Eisenberg LM, Bhalerao J, Jenkins NA, Copeland NG, Osborne MP, Bowcock AM, Brown AM; 1997; Genomics 46:450-8). The Wnt gene family consists of at least 15 structurally related genes that encode secreted extracellular signaling factors. Wnt signaling is involved in many mammalian developmental processes, including cell proliferation, differentiation and epithelial-mesenchymal interactions, through which they contribute to the development of tissues and organs such as the limbs, the brain, the reproductive tract and the kidney. Evidence from tumor expression studies and transgenic animals experiments suggests that inappropriate activation of the Wnt signaling pathway is a major feature in human neoplasia and that oncogenic activation of this pathway can occur at many levels. Inappropriate expression of	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, and inflammation

	the Wnt ligand and Wnt binding proteins have been found in a variety of human tumors (Smalley MJ, Dale TC;1999; Cancer Metastasis Rev 18:215-30).	
sbg236015LIPASE	An embodiment of the invention is the use of sbg236015LIPASE for treating lipase deficiency. A close homologue of sbg236015LIPASE is lysosomal acid lipase. The lysosomal acid lipase catalyzes the deacylation of triacylglyceryl and cholesteryl ester core lipids of endocytosed low density lipoproteins. This activity is deficient in patients with Wolman disease and cholesteryl ester storage disease, which are caused by a deficiency of lysosomal acid lipase activity, resulting in massive accumulation of cholesteryl ester and triglycerides (Anderson RA, Sando GN; 1991;J Biol Chem 266:22479-84).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, Wolman disease, and cholesteryl ester storage disease
sbg417005LAMININ_ALPHA	An embodiment of the invention is the use of sbg417005LAMININ_ALPHA to promote myogenesis in skeletal muscle, outgrowth of neurites from central and peripheral neurons, and mesenchymal to epithelial transitions in kidney. A close homologue of sbg417005LAMININ_ALPHA is laminin. Laminins trimers, composed of alpha, beta, and gamma chains, are components of all basal laminae (BLs) throughout the bodies. In mammals they play at least three essential roles. First, they are major structural elements of BLs, forming one of two self-assembling networks to which other glycoproteins and proteoglycans of the BL attach. Second, they interact with cell surface components such as dystroglycan to attach cells to the extracellular matrix. Third, they are signaling molecules that interact with cellular receptors such as the integrins to convey important information to the cell interior. The alpha chains are ligands for most cellular laminin receptors. (Miner JH, Patton BL, Lentz SI, Gilbert DJ, Snider WD, Jenkins NA, Copeland NG, Sanes JR; 1997; J Cell Biol 137:685-701).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, congenital muscular dystrophy, and junctional epidermolysis bullosa
sbg425649KINASEa	An embodiment of the invention is the use of sbg425649KINASEa in DNA replication and repair, membrane trafficking, neuroprotective, cytostatic, cardioactive, immunomodulatory, muscular, vulnerary, gastrointestinal, nephrotropic, anti-infective, gynaecological and antibacterial activities, and can be used in gene therapy. Close homologues of sbg425649KINASEa is mammalian casein kinases I (CKI) and human prostate cancer associated protein. CKI belongs to a family of serine/threonine protein kinases involved in diverse cellular processes including DNA replication and repair, membrane trafficking, circadian rhythms and Wnt signaling. Human prostate cancer associated proteins have neuroprotective, cytostatic, cardioactive, immunomodulatory, muscular, vulnerary, gastrointestinal, nephrotropic, anti-infective, gynaecological and antibacterial activities, and can be used in gene therapy.	Cancer, wound healing disorders, autoimmune disorders, hematopoietic disorders and infection

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg419582PROTOCADHERIN	An embodiment of the invention is the use of sbg419582PROTOCADHERIN in functional systems of the nervous system, and may be involved in the formation of the neural network. A close homologue of sbg419582PROTOCADHERIN is protocadherin. The expression of protocadherin is developmentally regulated in a subset of the functional systems of the nervous system, and may be involved in the formation of the neural network by segregation of the brain nuclei and mediation of the axonal connections (Hirano S, Yan Q, Suzuki ST; 1999; J Neurosci 19:995-1005). The members of the cadherin superfamily are divided into two groups: classical cadherin type and protocadherin type. The current cadherins appear to have evolved from protocadherin (Suzuki ST; 1996; J Cell Sci 109:2609-11).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, Parkinson's disease, Huntington's chorea, and multiple sclerosis
sbg453915TECTORINa	An embodiment of the invention is the use of sbg453915TECTORINa, a secreted protein, in cellular adhesion. A close homologue of sbg453915TECTORINa is mouse tectorin beta. The beta-tectorin is a protein of 36,074 Da that contains 4 consensus N glycosylation sites and a single zona pellucida domain. It is similar to components of the sperm-egg adhesion system, and, as such may have a similar functional role (Legan PK, Rau A, Keen JN, Richardson GP, The mouse tectorins. Modular matrix proteins of the inner ear homologous to components of the sperm-egg adhesion system. J Biol Chem 1997 Mar 28;272(13):8791-801).	Infection, cancer, wound healing disorders, hemotopoietic disorders and autoimmune disorders.
SBh385630.antiinflam	An embodiment of the invention is the use of SBh385630.antiinflam in gene therapy and are also suggested to have cytokine and cell proliferation/differentiation activity, immune stimulating (e.g.vaccines) or suppressing activity, haematopoiesis regulating activity, tissue growth activity, activin/inhibinactivity, chemotactic/chemokinetic activity, haemostatic and thrombolytic activity, receptor/ligand activity,anti-inflammatory activity, cadherin/tumour invasion suppressor activity, and tumour inhibition activity. Lipases are also reported to be useful for gene therapy (WO9957132-A1;.Agostino, M.J., filed by GENETICS INST INC.). Close homologues of SBh385630.antiinflam include lipases.	Lematopoietic disorders, wound healing disorders, viral and bacterial infections, cancer, and autoimmune diseases
sbg471005nAChR	An embodiment of the invention is the use of sbg471005nAChR in physiological and behavioural processes of the brain. A close homologue of sbg471005nAChR is neuronal nicotinic acetylcholine receptors. Neuronal nicotinic acetylcholine receptors are a family of ion channels which are widely distributed in the human brain. There are many subtypes, and each has individual pharmacological and functional profiles. They mediate the effects of nicotine, and are involved in a number of physiological and behavioural processes. Additionally they may be implicated in a number of pathological conditions such	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, Alzheimer's disease, Parkinson's disease, and schizophrenia

	as Alzheimer's disease, Parkinson's disease and schizophrenia (Paterson D, Nordberg A; 2000; Prog Neurobiol 61:75-111).	
sbg442445PROa	An embodiment of the invention is the use of sbg442445PROa which may be involved in protein-protein interation and signal transduction in immune system. sbg442445PROa was expressed predominantly in lung and spleen/lymph. It encodes a protein with leucine rich repeats which may be involved in protein-protein interation and signal transduction in immune systems.	Inflammation, autoimmune disorders, asthma, allergies and sbg442445PROa-associated disorders
sbg456548CytoRa	The present gene has been cloned. Sybrman data showed its high expression levels in placenta and moderate levels in spleen and lymph. A close homologue of sbg456548CytoRa is another Class II cytokine receptor, ZCYTOR7. An embodiment of the invention is the use of sbg456548CytoRa, a decoy receptor, in the identification of other ligands, the promotion of anti-microbial activation of these cells, and/or potentiate the effectiveness of the natural ligand. Growth factors are known to promote the progression of cancer. A decoy receptor could interfere with that process. Proliferation, survival and differentiation can be transduced from activated cytokine receptors (Cell Signal. 1998. 10(9):619-628). Blocking these events could be crucial in modulating various diseases. The decoy receptor could potentially interfere with binding of these or other putative ligands, preventing downstream effects (Blood. 1999. 94(6):1943-1951). GM-CSF also has anti-apoptotic activity. A decoy receptor might then be able to block GM-CSF's anti-apoptotic actions when appropriate (Mol Biol Cell. 1999. 10(11):3959-3970). Roles for blocking the activity of the decoy receptor can be envisioned. GM-CSF promotes anti-microbial functions of mature neutrophils. Inhibiting the activity of an interfering decoy receptor could promote anti-microbial activation of these cells. Furthermore, rhGM-CSF is in wide clinical use to fight acute myeloid leukemia (Haematologica. 1991. 82(2): 239-245). Inhibition of a decoy receptor could potentiate the effectiveness of the natural ligand.	Chronic and acute inflammation, allergy, arthritis (including rheumatoid arthritis), septicemia, autoimmune diseases (e.g., inflammatory bowel disease, psoriasis), transplant rejection, graft vs. host disease, infection, stroke, ischemia, acute respiratory disease syndrome, asthma, restenosis, brain injury, AIDS, bone diseases, cancer, atheroschlerosis, Alzheimers disease, , hematopoietic disorder, and wound healing disorder
sbg442358PROa	An embodiment of the invention is the use of sbg442358PROa useful in the prevention and treatment of cancers, cell proliferation, cardiovascular, reproductive, immune, musculoskeletal, developmental and gastrointestinal disorders and inflammation. Close homologues of sbg442358PROa are human protein B27231 and Drosophila LRR47 that also contains leucine-rich repeats (LRRs) motifs. LRR has been found in a variety of extracellular, membrane and cytoplasmic proteins.and are believed to mediate specific protein-protein interactions and to function in cellular adhesion (Ntwasa,M., Buchanan,S.G. and Gay,N.J. Biochim. Biophys. Acta 1218 (2), 181-186 (1994)).	Cancer, autoimmune disorders, hemotopoietic disorders, wound healing disorders and infections

Table IV. Quantitative, Tissue-specific mRNA expression detected using SybrMan

Quantitative, tissue-specific, mRNA expression patterns of the genes were measured using SYBR-Green Quantitative PCR (Applied Biosystems, Foster City, CA; see Schmittgen T.D. et al., Analytical Biochemistry 285:194-204, 2000) and human cDNAs prepared from various human tissues. Gene-specific PCR primers were designed using the first nucleic acid sequence listed in the Sequence List for each gene. Results are presented as the number of copies of each specific gene's mRNA detected in 1ng mRNA pool from each tissue. Two replicate mRNA measurements were made from each tissue RNA.

Gene Name sbg237163LIPASE

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. ± range for 2 data points per tissue)						
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine
sbg23716 3LIPASE	5 ±0	8 ±2	7 ±2	-6 ±1	5 ±1	5 ±2	4 ±6

Gene Name sbg237163LIPASE cont.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. ± range for 2 data points per tissue)			
	Spleen/lymph	Placenta	Testis	
sbg23716 3LIPASE	3 ±2	1 ±1	47 ±1	

Gene Name sbg251170CEAa

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. ± range for 2 data points per tissue)						
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine
sbg25117 0CEAa	3 ±1	19 ±1	30 ±5	-5 ±3	3 ±1	5 ±5	21 ±2

Gene Name sbg251170CEAa cont.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. ± range for 2 data points per tissue)			
	Spleen/lymph	Placenta	Testis	
sbg23716 3LIPASE	33 ±4	22 ±3	14 ±0	

Table IV (cont).

In each gene's first subset table, two replicate measurements of gene of identification (GOI) mRNA were measured from various human tissues (column 2 and 3). The average GOI mRNA copies of the two replicates were made from each tissue RNA (column 4). The average amount of 18S rRNA from each tissue RNA was measured (column 5) and used for normalization. To make each tissue

with the same amount of 50 ng of 18S rRNA, the normalization factor (column 6) was calculated by dividing 50 ng with the amount of 18S rRNA measured from each tissue (column 5). The mRNA copies per 50 ng of total RNA were obtained by multipling each GOI normalization factor and average mRNA copies (column7).

Fold changes shown in each gene's second subset table were only calculated for disease tissues which have a normal counterpart. There are blanks in the fold change column for all samples that do not have counterparts. In addition, the fold change calculations are the fold change in the disease sample as compared to the normal sample. Accordingly, there will not be a fold change calculation next to any of the normal samples. For patient matched cancer pairs (colon, lung, and breast), each tumor is compared to its specific normal counterpart. When patient-matched normal/disease pairs do not exist, each disease sample was compared back to the average of all the normal samples of that same tissue type. For example, normal brain from the same patient that provided Alzheimer's brain is not applicable . Three normal brain samples and 4 Alzheimer's brain samples are used in the fold change. Three normal samples were averaged, and each of the Alzheimer's samples was compared back to that average.

Abbreviations

ALZ Alzheimer's Disease
CT CLONTECH (1020 East Meadow Circle Palo Alto, CA 94303-4230, USA)
KC Sample prepared by GSK investigator
COPD chronic obstructive pulmonary disease
endo endothelial
VEGF vascular endothelial growth factor
bFGF basic fibroblast growth factor
BM bone marrow
osteo osteoblast
OA osteoarthritis
RA rheumatoid arthritis
PBL peripheral blood lymphocytes
PBMNC peripheral blood mononuclear cells
HIV human immunodeficiency virus
HSV Herpes simplex virus
HPV human papilloma virus

Gene Name sbg389686WNT15a

Strong expression in Brain and dendritic cells. Brain expression may be from presence of glial cells. Expression in RA and OA synovium along with dendritic cells suggests a role for this protein in these diseases. Down regulation in ischemic and dilated heart indicates that replacement of protein could be therapeutic.

Sample sbg389686WNT15a	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	0.00	0.00	3.06	16.34	0.00
Subcutaneous Adipose Zenbio	0.00	1.71	0.86	0.96	52.36	44.76
Adrenal Gland Clontech	2.29	4.18	3.24	0.61	81.97	265.16
Whole Brain Clontech	698.52	625.01	661.77	7.24	6.91	4570.20
Fetal Brain Clontech	4.14	6.78	5.46	0.48	103.95	567.57

Cerebellum Clontech	2.02	3.63	2.83	2.17	23.04	65.09
Cervix	3.16	10.14	6.65	2.42	20.66	137.40
Colon	2.48	3.44	2.96	2.71	18.45	54.61
Endometrium	2.69	5.20	3.95	0.73	68.21	269.10
Esophagus	10.67	3.24	6.96	1.37	36.50	253.83
Heart Clontech	9.26	6.07	7.67	1.32	37.88	290.34
Hypothalamus	7.10	5.16	6.13	0.32	155.28	951.86
Ileum	2.04	10.37	6.21	2.58	19.38	120.25
Jejunum	36.78	27.16	31.97	6.60	7.58	242.20
Kidney	16.46	16.55	16.51	2.12	23.58	389.27
Liver	14.07	3.34	8.71	1.50	33.33	290.17
Fetal Liver Clontech	4.60	8.89	6.75	10.40	4.81	32.43
Lung	3.11	10.49	6.80	2.57	19.46	132.30
Mammary Gland Clontech	3.28	10.61	6.95	13.00	3.85	26.71
Myometrium	1.79	13.84	7.82	2.34	21.37	166.99
Omentum	1.96	2.65	2.31	3.94	12.69	29.25
Ovary	4.50	1.71	3.11	4.34	11.52	35.77
Pancreas	3.40	2.41	2.91	0.81	61.80	179.54
Head of Pancreas	2.22	4.63	3.43	1.57	31.85	109.08
Parotid Gland	5.48	2.07	3.78	5.48	9.12	34.44
Placenta Clontech	15.15	12.80	13.98	5.26	9.51	132.84
Prostate	3.39	7.44	5.42	3.00	16.67	90.25
Rectum	2.98	3.94	3.46	1.23	40.65	140.65
Salivary Gland Clontech	3.24	1.61	2.43	7.31	6.84	16.59
Skeletal Muscle Clontech	2.01	1.55	1.78	1.26	39.68	70.63
Skin	2.69	3.45	3.07	1.21	41.32	126.86
Small Intestine Clontech	5.39	1.67	3.53	0.98	51.07	180.29
Spleen	3.96	2.52	3.24	4.92	10.16	32.93
Stomach	1.08	5.33	3.21	2.73	18.32	58.70
Testis Clontech	3.27	2.88	3.08	0.57	87.87	270.21
Thymus Clontech	5.43	4.42	4.93	9.89	5.06	24.90
Thyroid	2.32	3.01	2.67	2.77	18.05	48.10
Trachea Clontech	1.64	4.25	2.95	9.71	5.15	15.16
Urinary Bladder	3.63	6.81	5.22	5.47	9.14	47.71
Uterus	31.55	11.10	21.33	5.34	9.36	199.67

Sample sbg389686WNT15a	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	36.16	72.32	colon normal	
colon tumor GW98-166	21940	71.5	143.00	colon tumor	1.977323009
colon normal GW98-178	22080	2.09	4.18	colon normal	
colon tumor GW98-177	22060	9.84	19.68	colon tumor	4.708133971
colon normal GW98-561	23514	13.09	26.18	colon normal	
colon tumor GW98-560	23513	15.11	30.22	colon tumor	1.154316272
colon normal GW98-894	24691	8.62	17.24	colon normal	
colon tumor GW98-893	24690	5.76	11.52	colon tumor	-1.496527778
lung normal GW98-3	20742	140.19	280.38	lung normal	
lung tumor GW98-2	20741	1.67	3.34	lung tumor	-83.94610778
lung normal GW97-179	20677	60.54	121.08	lung normal	
lung tumor GW97-178	20676	135.62	271.24	lung tumor	2.240171787
lung normal GW98-165	21922	257.96	515.92	lung normal	
lung tumor GW98-164	21921	61.69	123.38	lung tumor	-4.181552926
lung normal GW98-282	22584	49.3	98.60	lung normal	
lung tumor GW98-281	22583	12.39	24.78	lung tumor	-3.979015335
breast normal GW00-392	28750	71.94	71.94	breast normal	
breast tumor GW00-391	28746	41.4	82.80	breast tumor	1.150959133
breast normal GW00-413	28798	19.37	19.37	breast normal	
breast tumor GW00-412	28797	1.13	2.26	breast tumor	-8.57079646
breast normal GW00-235:238	27592-95	8.19	8.19	breast normal	
breast tumor GW00-231:234	27588-91	38.27	38.27	breast tumor	4.672771673
breast normal GW98-621	23656	77.26	154.52	breast normal	
breast tumor GW98-620	23655	37.57	75.14	breast tumor	-2.056428001
brain normal BB99-542	25507	597.17	1194.34	brain normal	
brain normal BB99-406	25509	104.34	208.68	brain normal	
brain normalBB99-904	25546	282.15	564.30	brain normal	
brain stage 5 ALZ BB99-874	25502	84.26	168.52	brain stage 5 ALZ	-3.891367988
brain stage 5 ALZ BB99-887	25503	247.01	494.02	brain stage 5 ALZ	-1.327422641
brain stage 5 ALZ BB99-862	25504	173.02	346.04	brain stage 5 ALZ	-1.895079567
brain stage 5 ALZ BB99-927	25542	253.73	507.46	brain stage 5 ALZ	-1.292266057
CT lung KC	normal	146.22	292.44	CT lung	
lung 26 KC	normal	150.46	150.46	lung 26	
lung 27 KC	normal	0	0.00	lung 27	
lung 24 KC	COPD	4.76	4.76	lung 24	-23.36292017
lung 28 KC	COPD	10.06	10.06	lung 28	-11.05442346
lung 23 KC	COPD	2.75	2.75	lung 23	-40.43909091

lung 25 KC	COPD	1.93	1.93	lung 25	
asthmatic lung ODO3112	29321	20.88	20.88	asthmatic lung	-5.326029693
asthmatic lung ODO3433	29323	133.29	266.58	asthmatic lung	2.397140481
asthmatic lung ODO3397	29322	322.77	645.54	asthmatic lung	5.804824315
asthmatic lung ODO4928	29325	43.52	87.04	asthmatic lung	-1.277659697
endo cells KC	control	1.89	1.89	endo cells	
endo VEGF KC		0	0.00	endo VEGF	-1.89
endo bFGF KC		1.17	1.17	endo bFGF	-1.615384615
heart Clontech	normal	153.9	307.80	heart	
heart (T-1) ischemic	29417	137.74	275.48	heart T-1	-1.117322492
heart (T-14) non-obstructive DCM	29422	87.79	175.58	heart T-14	-1.753047044
heart (T-3399) DCM	29426	43.68	87.36	heart T-3399	-3.523351648
adenoid GW99-269	26162	17.62	35.24	adenoid	
tonsil GW98-280	22582	52.34	104.68	tonsil	
T cells PC00314	28453	8.45	16.90	T cells	
PBMNC KC		1.99	1.99	PBMNC	
monocyte KC		4.74	9.48	monocyte	
B cells PC00665	28455	7.65	15.30	B cells	
dendritic cells 28441		194.97	389.94	dendritic cells	
neutrophils	28440	2.13	2.13	neutrophils	
eosinophils	28446	7.25	14.50	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		0	0.00	BM stim	0
osteo dif KC		1.48	1.48	osteo dif	
osteo undif KC		7.41	7.41	osteo undif	5.006756757
chondrocytes		26.64	66.60	chondrocytes	
OA Synovium IP12/01	29462	476.3	476.30	OA Synovium	
OA Synovium NP10/01	29461	151.36	302.72	OA Synovium	
OA Synovium NP57/00	28464	165.01	330.02	OA Synovium	
RA Synovium NP03/01	28466	84.02	168.04	RA Synovium	
RA Synovium NP71/00	28467	184.75	369.50	RA Synovium	
RA Synovium NP45/00	28475	223.3	446.60	RA Synovium	
OA bone (biobank)	29217	72.31	72.31	OA bone (biobank)	
OA bone Sample 1	J. Emory	10.46	20.92	OA bone	
OA bone Sample 2	J. Emory	111.79	223.58	OA bone	
Cartilage (pool)	Normal	215.54	431.08	Cartilage (pool)	
Cartilage (pool)	OA	81.85	163.70	Cartilage (pool)	-2.633353696

PBL unifected	28441	2.31	4.62	PBL unifected	
PBL HIV IIIB	28442	2.28	4.56	PBL HIV IIIB	-1.013157895
MRC5 uninfected (100%)	29158	2.37	4.74	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	37.5	75.00	MRC5 HSV strain F	15.82278481
W12 cells	29179	0.93	1.86	W12 cells	
Keratinocytes	29180	1.33	2.66	Keratinocytes	

Gene Name sbg389686WNT15a

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	1.98
colon tumor	4.71
colon tumor	1.15
colon tumor	-1.50
lung tumor	-83.95
lung tumor	2.24
lung tumor	-4.18
lung tumor	-3.98
breast tumor	1.15
breast tumor	-8.57
breast tumor	4.67
breast tumor	-2.06
brain stage 5 ALZ	-3.89
brain stage 5 ALZ	-1.33
brain stage 5 ALZ	-1.90
brain stage 5 ALZ	-1.29
lung 24	-23.36
lung 28	-11.05
lung 23	-40.44
asthmatic lung	-5.33
asthmatic lung	2.40
asthmatic lung	5.80
asthmatic lung	-1.28
endo VEGF	-1.89
endo bFGF	-1.62
heart T-1	-1.12
heart T-14	-1.75
heart T-3399	-3.52
BM stim	0.00
osteo undif	5.01
Cartilage (pool)	-2.63
PBL HIV IIIB	-1.01
MRC5 HSV strain F	15.82

Gene Name sbg236015LIPASE

Strongly expressed in neutrophils and eosinophils suggesting an immune system function. Additional expression is seen in RA and OA synovium and1/3 OA bone samples. This suggests an involvement of 236015 in RA and OA. The high expression in skin when taken together with expression in neutrophils and eosinophils suggests possible involvement in immune pathologies of the skin ie. Eosinophilia, psoriasis and eczema. The expression in eosinophils also suggests involvement in allergic reactions. Expression in neutrophils suggests role in anti-infectives.

Sample sbg236015LIPASE	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	11.45	5.73	3.06	16.34	93.55
Subcutaneous Adipose Zenbio	0.00	1.33	0.67	0.96	52.36	34.82
Adrenal Gland Clontech	0.52	5.04	2.78	0.61	81.97	227.87
Whole Brain Clontech	15.73	14.55	15.14	7.24	6.91	104.56
Fetal Brain Clontech	1.02	0.94	0.98	0.48	103.95	101.87
Cerebellum Clontech	0.38	0.39	0.39	2.17	23.04	8.87
Cervix	16.33	20.03	18.18	2.42	20.66	375.62
Colon	32.41	50.89	41.65	2.71	18.45	768.45
Endometrium	0.40	0.42	0.41	0.73	68.21	27.97
Esophagus	5.45	22.47	13.96	1.37	36.50	509.49
Heart Clontech	0.92	0.00	0.46	1.32	37.88	17.42
Hypothalamus	0.50	1.59	1.05	0.32	155.28	162.27
Ileum	41.95	1.51	21.73	2.58	19.38	421.12
Jejunum	7.59	15.40	11.50	6.60	7.58	87.08
Kidney	5.32	6.82	6.07	2.12	23.58	143.16
Liver	12.64	19.46	16.05	1.50	33.33	535.00
Fetal Liver Clontech	10.02	5.90	7.96	10.40	4.81	38.27
Lung	22.86	24.78	23.82	2.57	19.46	463.42
Mammary Gland Clontech	1.53	20.56	11.05	13.00	3.85	42.48
Myometrium	16.05	1.34	8.70	2.34	21.37	185.79
Omentum	8.33	9.88	9.11	3.94	12.69	115.55
Ovary	8.22	14.40	11.31	4.34	11.52	130.30
Pancreas	0.00	1.58	0.79	0.81	61.80	48.83
Head of Pancreas	0.00	1.98	0.99	1.57	31.85	31.53
Parotid Gland	5.30	11.45	8.38	5.48	9.12	76.41
Placenta Clontech	11.93	1.22	6.58	5.26	9.51	62.50
Prostate	0.00	0.00	0.00	3.00	16.67	0.00
Rectum	6.96	1.27	4.12	1.23	40.65	167.28
Salivary Gland Clontech	0.34	0.53	0.44	7.31	6.84	2.98
Skeletal Muscle Clontech	176.88	0.41	88.65	1.26	39.68	3517.66

Skin	95.17	147.16	121.17	1.21	41.32	5006.82
Small Intestine Clontech	0.35	1.31	0.83	0.98	51.07	42.39
Spleen	105.73	80.76	93.25	4.92	10.16	947.61
Stomach	0.56	3.73	2.15	2.73	18.32	39.29
Testis Clontech	0.79	0.78	0.79	0.57	87.87	68.98
Thymus Clontech	22.00	22.48	22.24	9.89	5.06	112.44
Thyroid	0.65	0.48	0.57	2.77	18.05	10.20
Trachea Clontech	1.20	0.00	0.60	9.71	5.15	3.09
Urinary Bladder	5.59	8.67	7.13	5.47	9.14	65.17
Uterus	19.26	27.10	23.18	5.34	9.36	217.04

Sample sbg236015LIPASE	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	58.7	117.40	colon normal	
colon tumor GW98-166	21940	300.92	601.84	colon tumor	5.126405451
colon normal GW98-178	22080	8.78	17.56	colon normal	
colon tumor GW98-177	22060	23.74	47.48	colon tumor	2.703872437
colon normal GW98-561	23514	27.1	54.20	colon normal	
colon tumor GW98-560	23513	39.16	78.32	colon tumor	1.44501845
colon normal GW98-894	24691	10.15	20.30	colon normal	
colon tumor GW98-893	24690	144.58	289.16	colon tumor	14.24433498
lung normal GW98-3	20742	165.8	331.60	lung normal	
lung tumor GW98-2	20741	80.9	161.80	lung tumor	-2.049443758
lung normal GW97-179	20677	37.81	75.62	lung normal	
lung tumor GW97-178	20676	109.72	219.44	lung tumor	2.90187781
lung normal GW98-165	21922	150.06	300.12	lung normal	
lung tumor GW98-164	21921	169.73	339.46	lung tumor	1.131080901
lung normal GW98-282	22584	489.42	978.84	lung normal	
lung tumor GW98-281	22583	188.22	376.44	lung tumor	-2.600255021
breast normal GW00-392	28750	44.86	44.86	breast normal	
breast tumor GW00-391	28746	46.35	92.70	breast tumor	2.06642889
breast normal GW00-413	28798	16.35	16.35	breast normal	
breast tumor GW00-412	28797	55.98	111.96	breast tumor	6.847706422
breast normal GW00-235:238	27592-95	3.84	3.84	breast normal	
breast tumor GW00-231:234	27588-91	35.8	35.80	breast tumor	9.322916667
breast normal GW98-621	23656	12.14	24.28	breast normal	
breast tumor GW98-620	23655	44.85	89.70	breast tumor	3.694398682
brain normal BB99-542	25507	26.03	52.06	brain normal	
brain normal BB99-406	25509	14.78	29.56	brain normal	
brain normal BB99-904	25546	3.39	6.78	brain normal	
brain stage 5 ALZ BB99-874	25502	35.71	71.42	brain stage 5 ALZ	2.423755656

brain stage 5 ALZ BB99-887	25503	9.11	18.22	brain stage 5 ALZ	-1.617270399
brain stage 5 ALZ BB99-862	25504	8.18	16.36	brain stage 5 ALZ	-1.801140994
brain stage 5 ALZ BB99-927	25542	46.37	92.74	brain stage 5 ALZ	3.147285068
CT lung KC	normal	80.77	161.54	CT lung	
lung 26 KC	normal	233.65	233.65	lung 26	
lung 27 KC	normal	75.27	75.27	lung 27	
lung 24 KC	COPD	68.64	68.64	lung 24	-1.876821096
lung 28 KC	COPD	94.1	94.10	lung 28	-1.369022317
lung 23 KC	COPD	88.48	88.48	lung 23	-1.455978752
lung 25 KC	normal	44.84	44.84	lung 25	
asthmatic lung ODO3112	29321	111.42	111.42	asthmatic lung	-1.156210734
asthmatic lung ODO3433	29323	566.5	1133.00	asthmatic lung	8.794876771
asthmatic lung ODO3397	29322	262.77	525.54	asthmatic lung	4.079487677
asthmatic lung ODO4928	29325	367.52	735.04	asthmatic lung	5.70572482
endo cells KC	control	3.23	3.23	endo cells	
endo VEGF KC		3.41	3.41	endo VEGF	1.055727554
endo bFGF KC		0	0.00	endo bFGF	-3.23
heart Clontech	normal	0	0.00	heart	
heart (T-1) ischemic	29417	35.96	71.92	heart T-1	71.92
heart (T-14) non-obstructive DCM	29422	18.72	37.44	heart T-14	37.44
heart (T-3399) DCM	29426	37.97	75.94	heart T-3399	75.94
adenoid GW99-269	26162	14.17	28.34	adenoid	
tonsil GW98-280	22582	51.21	102.42	tonsil	
T cells PC00314	28453	111.1	222.20	T cells	
PBMNC KC		162.01	162.01	PBMNC	
monocyte KC		90.49	180.98	monocyte	
B cells PC00665	28455	109.71	219.42	B cells	
dendritic cells 28441		2.44	4.88	dendritic cells	
neutrophils	28440	1110.91	1110.91	neutrophils	
eosinophils	28446	835.72	1671.44	eosinophils	
BM unstim KC		181.05	181.05	BM unstim	
BM stim KC		93.96	93.96	BM stim	-1.92688378
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0.72	0.72	osteo undif	0.72
chondrocytes		2.03	5.08	chondrocytes	
OA Synovium IP12/01	29462	27.82	27.82	OA Synovium	
OA Synovium NP10/01	29461	84.94	169.88	OA Synovium	
OA Synovium NP57/00	28464	46.58	93.16	OA Synovium	
RA Synovium NP03/01	28466	248.24	496.48	RA Synovium	

RA Synovium NP71/00	28467	148.32	296.64	RA Synovium	
RA Synovium NP45/00	28475	260.28	520.56	RA Synovium	
OA bone (biobank)	29217	10.27	10.27	OA bone (biobank)	
OA bone Sample 1	J. Emory	17.32	34.64	OA bone	
OA bone Sample 2	J. Emory	657.01	1314.02	OA bone	
Cartilage (pool)	Normal	59.17	118.34	Cartilage (pool)	
Cartilage (pool)	OA	23.33	46.66	Cartilage (pool)	-2.53621946
PBL unifected	28441	23.51	47.02	PBL unifected	
PBL HIV IIIB	28442	5.86	11.72	PBL HIV IIIB	-4.011945392
MRC5 uninfected (100%)	29158	3.79	7.58	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	80.19	160.38	MRC5 HSV strain F	21.15831135
W12 cells	29179	95.42	190.84	W12 cells	
Keratinocytes	29180	16.18	32.36	Keratinocytes	

Gene Name sbg236015LIPASE

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	5.13
colon tumor	2.70
colon tumor	1.45
colon tumor	14.24
lung tumor	-2.05
lung tumor	2.90
lung tumor	1.13
lung tumor	-2.60
breast tumor	2.07
breast tumor	6.85
breast tumor	9.32
breast tumor	3.69
brain stage 5 ALZ	2.42
brain stage 5 ALZ	-1.62
brain stage 5 ALZ	-1.80
brain stage 5 ALZ	3.15
lung 24	-1.88
lung 28	-1.37
lung 23	-1.46
asthmatic lung	-1.16
asthmatic lung	8.79
asthmatic lung	4.08
asthmatic lung	5.71
endo VEGF	1.06

endo bFGF	-3.23
heart T-1	71.92
heart T-14	37.44
heart T-3399	75.94
BM stim	-1.93
osteo undif	0.72
Cartilage (pool)	-2.54
PBL HIV IIIB	-4.01
MRC5 HSV strain F	21.16

Gene Name sbg417005LAMININ

Expression in adenoid, tonsil and B-cells with corroborating expression in RA/OA samples and asthmatic lung (1/4) suggests involvement in these diseases. Strong expression in brain with overexpression in Alzheimer's disease indicates a role in AD. Down regulation in HSV infected cells suggests potential host cell factor. Expression in colon and lung normal/tumor pairs without corroborating expression in normal tissues suggests immune cell infiltrates.

Sample sbg417005LAMININ	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/50 ng total RNA**
Subcutaneous Adipocytes Zenbio	60.2785303	73.59679955	66.94	3.06	16.34	1093.75
Subcutaneous Adipose Zenbio	3.032572965	1.985862153	2.51	0.96	52.36	131.37
Adrenal Gland Clontech	0.965703497	0.965703497	0.97	0.61	81.97	79.16
Whole Brain Clontech	4131.557992	6997.879078	5564.72	7.24	6.91	38430.38
Fetal Brain Clontech	0.965703497	3.268211325	2.12	0.48	103.95	220.06
Cerebellum Clontech	3.301057867	17.3966665	10.35	2.17	23.04	238.45
Cervix	5.920484049	7.517891571	6.72	2.42	20.66	138.83
Colon	35.48962684	22.53180605	29.01	2.71	18.45	535.25
Endometrium	11.59757492	0.965703497	6.28	0.73	68.21	428.49
Esophagus	7.098528857	3.523216475	5.31	1.37	36.50	193.83
Heart Clontech	0.965703497	5.368977287	3.17	1.32	37.88	119.98
Hypothalamus	0.965703497	0.965703497	0.97	0.32	155.28	149.95
Ileum	30.81006847	14.15032296	22.48	2.58	19.38	435.66
Jejunum	44.08994058	30.29386314	37.19	6.60	7.58	281.76
Kidney	9.424973981	15.68529125	12.56	2.12	23.58	296.11
Liver	3.742288161	0.965703497	2.35	1.50	33.33	78.47
Fetal Liver Clontech	94.45949484	93.8962252	94.18	10.40	4.81	452.78
Lung	13.84782444	19.95367566	16.90	2.57	19.46	328.81
Mammary Gland Clontech	107.7956161	95.02632495	101.41	13.00	3.85	390.04
Myometrium	12.50117866	14.93742804	13.72	2.34	21.37	293.15
Omentum	13.998213	22.03816357	18.02	3.94	12.69	228.66
Ovary	0.965703497	0.965703497	0.97	4.34	11.52	11.13
Pancreas	2.254750425	0.965703497	1.61	0.81	61.80	99.52

Head of Pancreas	0.965703497	0.965703497	0.97	1.57	31.85	30.75
Parotid Gland	25.8930892	14.85668173	20.37	5.48	9.12	185.90
Placenta Clontech	83.84029668	95.02632495	89.43	5.26	9.51	850.13
Prostate	8.047386733	15.18245262	11.61	3.00	16.67	193.58
Rectum	10.53572882	20.06385011	15.30	1.23	40.65	621.94
Salivary Gland Clontech	62.43024331	57.19623352	59.81	7.31	6.84	409.12
Skeletal Muscle Clontech	1.376746214	0.965703497	1.17	1.26	39.68	46.48
Skin	0.965703497	0.965703497	0.97	1.21	41.32	39.91
Small Intestine Clontech	0.965703497	0.965703497	0.97	0.98	51.07	49.32
Spleen	0.965703497	5.740147492	3.35	4.92	10.16	34.07
Stomach	0.965703497	0.965703497	0.97	2.73	18.32	17.69
Testis Clontech	0.965703497	0.965703497	0.97	0.57	87.87	84.86
Thymus Clontech	258.7386545	207.7169358	233.23	9.89	5.06	1179.11
Thyroid	12.56849785	19.09489343	15.83	2.77	18.05	285.77
Trachea Clontech	24.35330878	31.87047641	28.11	9.71	5.15	144.76
Urinary Bladder	51.81831091	57.53035871	54.67	5.47	9.14	499.77
Uterus	13.12099559	14.61718971	13.87	5.34	9.36	129.86

Sample sbg417005LAMININ	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	15446.92728	30893.85	colon normal	
colon tumor GW98-166	21940	23910.90415	47821.81	colon tumor	1.547939193
colon normal GW98-178	22080	14621.97321	29243.95	colon normal	
colon tumor GW98-177	22060	2058.30396	4116.61	colon tumor	-7.10389403
colon normal GW98-561	23514	5590.900474	11181.80	colon normal	
colon tumor GW98-560	23513	12318.10362	24636.21	colon tumor	2.203241442
colon normal GW98-894	24691	4478.692403	8957.38	colon normal	
colon tumor GW98-893	24690	7546.100944	15092.20	colon tumor	1.684889308
lung normal GW98-3	20742	23910.90415	47821.81	lung normal	
lung tumor GW98-2	20741	35021.23317	70042.47	lung tumor	1.464655328
lung normal GW97-179	20677	23341.61421	46683.23	lung normal	
lung tumor GW97-178	20676	24103.90252	48207.81	lung tumor	1.032657909
lung normal GW98-165	21922	18374.41273	36748.83	lung normal	
lung tumor GW98-164	21921	34735.19726	69470.39	lung tumor	1.890411289
lung normal GW98-282	22584	3002.298467	6004.60	lung normal	
lung tumor GW98-281	22583	3519.560955	7039.12	lung tumor	1.172288829
breast normal GW00-392	28750	5978.671937	5978.67	breast normal	
breast tumor GW00-391	28746	5674.721186	11349.44	breast tumor	1.898321649
breast normal GW00-413	28798	1523.643258	1523.64	breast normal	
breast tumor GW00-412	28797	956.0902914	1912.18	breast tumor	1.255005444
breast normal GW00-	27592-95	760.6128764	760.61	breast	

235:238				normal	
breast tumor GW00-231:234	27588-91	4192.50003	4192.50	breast tumor	5.51200244
breast normal GW98-621	23656	5674.721186	11349.44	breast normal	
breast tumor GW98-620	23655	8017.202071	16034.40	breast tumor	1.412792243
brain normal BB99-542	25507	791.7818289	1583.56	brain normal	
brain normal BB99-406	25509	524.990001	1049.98	brain normal	
brain normal BB99-904	25546	396.8655236	793.73	brain normal	
brain stage 5 ALZ BB99-874	25502	3203.498645	6407.00	brain stage 5 ALZ	5.608243725
brain stage 5 ALZ BB99-887	25503	3925.505917	7851.01	brain stage 5 ALZ	6.872234505
brain stage 5 ALZ BB99-862	25504	1502.651942	3005.30	brain stage 5 ALZ	2.630635833
brain stage 5 ALZ BB99-927	25542	1555.711325	3111.42	brain stage 5 ALZ	2.723524884
CT lung KC	normal	3730.249874	7460.50	CT lung	
lung 26 KC	normal	286.3143862	286.31	lung 26	
lung 27 KC	normal	72.30560941	72.31	lung 27	
lung 24 KC	COPD	28.47771374	28.48	lung 24	-69.25877363
lung 28 KC	COPD	66.98006875	66.98	lung 28	-29.44654382
lung 23 KC	COPD	57.53035871	57.53	lung 23	-34.28331708
lung 25 KC	COPD	70.20637402	70.21	lung 25	
asthmatic lung ODO3112	29321	2304.915385	2304.92	asthmatic lung	1.168624722
asthmatic lung ODO3433	29323	3112.377018	6224.75	asthmatic lung	3.156038395
asthmatic lung ODO3397	29322	21892.2071	43784.41	asthmatic lung	22.19931768
asthmatic lung ODO4928	29325	5268.438364	10536.88	asthmatic lung	5.34234563
endo cells KC	control	396.8655236	396.87	endo cells	
endo VEGF KC		157.1987188	157.20	endo VEGF	-2.524610421
endo bFGF KC		518.1542863	518.15	endo bFGF	1.305616778
heart Clontech	normal	1865.302957	3730.61	heart	
heart (T-1) ischemic	29417	3757.505456	7515.01	heart T-1	2.014421005
heart (T-14) non-obstructive DCM	29422	1633.333543	3266.67	heart T-14	-1.142022072
heart (T-3399) DCM	29426	2938.226492	5876.45	heart T-3399	1.575200683
adenoid GW99-269	26162	1238.725105	2477.45	adenoid	
tonsil GW98-280	22582	2288.625236	4577.25	tonsil	
T cells PC00314	28453	61.34444995	122.69	T cells	
PBMNC KC		5.341492957	5.34	PBMNC	
monocyte KC		3.576686692	7.15	monocyte	
B cells PC00665	28455	716.2601536	1432.52	B cells	
dendritic cells 28441		32.23243314	64.46	dendritic cells	
neutrophils	28440	32.9693996	32.97	neutrophils	
eosinophils	28446	1.444144312	2.89	eosinophils	
BM unstim KC		5.951115795	5.95	BM unstim	

BM stim KC		11.72233235	11.72	BM stim	1.969770503
osteo dif KC		10.20495465	10.20	osteo dif	
osteo undif KC		8.526098078	8.53	osteo undif	-1.196907959
chondrocytes		14621.97321	36554.93	chondrocytes	
OA Synovium IP12/01	29462	5549.480142	5549.48	OA Synovium	
OA Synovium NP10/01	29461	3545.197127	7090.39	OA Synovium	
OA Synovium NP57/00	28464	4223.325454	8446.65	OA Synovium	
RA Synovium NP03/01	28466	1221.845309	2443.69	RA Synovium	
RA Synovium NP71/00	28467	4892.67872	9785.36	RA Synovium	
RA Synovium NP45/00	28475	1080.396739	2160.79	RA Synovium	
OA bone (biobank)	29217	995.7612933	995.76	OA bone (biobank)	
OA bone Sample 1	J. Emory	982.3483914	1964.70	OA bone	
OA bone Sample 2	J. Emory	472.8535333	945.71	OA bone	
Cartilage (pool)	Normal	1213.496434	2426.99	Cartilage (pool)	
Cartilage (pool)	OA	697.4302173	1394.86	Cartilage (pool)	-1.73995391
PBL unifected	28441	161.1142664	322.23	PBL unifected	
PBL HIV IIIB	28442	191.5686557	383.14	PBL HIV IIIB	1.189023542
MRC5 uninfected (100%)	29158	5934.220593	11868.44	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	50.63206269	101.26	MRC5 HSV strain F	-117.2028213
W12 cells	29179	13843.2955	27686.59	W12 cells	
Keratinocytes	29180	11849.9156	23699.83	Keratinocytes	

Gene Name sbg417005LAMININ

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	1.55
colon tumor	-7.10
colon tumor	2.20
colon tumor	1.68
lung tumor	1.46
lung tumor	1.03
lung tumor	1.89
lung tumor	1.17
breast tumor	1.90
breast tumor	1.26
breast tumor	5.51

breast tumor	1.41
brain stage 5 ALZ	5.61
brain stage 5 ALZ	6.87
brain stage 5 ALZ	2.63
brain stage 5 ALZ	2.72
lung 24	-69.26
lung 28	-29.45
lung 23	-34.28
asthmatic lung	1.17
asthmatic lung	3.16
asthmatic lung	22.20
asthmatic lung	5.34
endo VEGF	-2.52
endo bFGF	1.31
heart T-1	2.01
heart T-14	-1.14
heart T-3399	1.58
BM stim	1.97
osteo undif	-1.20
Cartilage (pool)	-1.74
PBL HIV IIIB	1.19
MRC5 HSV strain F	-117.20

Gene Name sbg425649KINASEa
Strongly expressed in neutrophils and eosinophils suggesting function in immume system such as involvement in allergic reactions and anti-infective. Lower expression in T-cells. Expression in 2/3 OA bone samples indicate a role in OA. Strongly expressed in rectum and skeletal muscle, unknown function.

Sample sbg425649KINASEa	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/ 50 ng total RNA**
Subcutaneous Adipocytes Zenbio	0.00	0.03	0.02	3.06	16.34	0.25
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	0.23	0.00	0.12	0.61	81.97	9.43
Whole Brain Clontech	163.64	47.63	105.64	7.24	6.91	729.52
Fetal Brain Clontech	0.47	0.00	0.24	0.48	103.95	24.43
Cerebellum Clontech	0.00	0.00	0.00	2.17	23.04	0.00
Cervix	5.54	0.00	2.77	2.42	20.66	57.23
Colon	0.70	0.00	0.35	2.71	18.45	6.46
Endometrium	0.33	0.06	0.20	0.73	68.21	13.30
Esophagus	0.35	0.47	0.41	1.37	36.50	14.96
Heart Clontech	0.00	0.00	0.00	1.32	37.88	0.00
Hypothalamus	0.00	0.00	0.00	0.32	155.28	0.00
Ileum	0.00	4.49	2.25	2.58	19.38	43.51
Jejunum	0.29	0.73	0.51	6.60	7.58	3.86
Kidney	0.00	0.00	0.00	2.12	23.58	0.00
Liver	10.48	5.64	8.06	1.50	33.33	268.67

Fetal Liver Clontech	8.56	0.00	4.28	10.40	4.81	20.58
Lung	0.00	0.00	0.00	2.57	19.46	0.00
Mammary Gland Clontech	0.00	0.00	0.00	13.00	3.85	0.00
Myometrium	8.61	5.00	6.81	2.34	21.37	145.41
Omentum	0.23	10.99	5.61	3.94	12.69	71.19
Ovary	4.48	4.62	4.55	4.34	11.52	52.42
Pancreas	0.27	0.00	0.14	0.81	61.80	8.34
Head of Pancreas	0.11	0.04	0.08	1.57	31.85	2.39
Parotid Gland	0.69	4.51	2.60	5.48	9.12	23.72
Placenta Clontech	10.58	0.14	5.36	5.26	9.51	50.95
Prostate	9.74	6.18	7.96	3.00	16.67	132.67
Rectum	225.51	76.99	151.25	1.23	40.65	6148.37
Salivary Gland Clontech	60.93	67.22	64.08	7.31	6.84	438.27
Skeletal Muscle Clontech	749.28	29.78	389.53	1.26	39.68	15457.54
Skin	0.00	4.46	2.23	1.21	41.32	92.15
Small Intestine Clontech	0.73	0.00	0.37	0.98	51.07	18.64
Spleen	4.10	8.60	6.35	4.92	10.16	64.53
Stomach	4.24	19.28	11.76	2.73	18.32	215.38
Testis Clontech	10.11	6.34	8.23	0.57	87.87	722.76
Thymus Clontech	2.79	5.35	4.07	9.89	5.06	20.58
Thyroid	0.00	0.06	0.03	2.77	18.05	0.54
Trachea Clontech	5.24	14.14	9.69	9.71	5.15	49.90
Urinary Bladder	0.09	0.00	0.05	5.47	9.14	0.41
Uterus	27.26	7.61	17.44	5.34	9.36	163.25

Sample sbg425649KINASEa	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	11.11	22.22	colon normal	
colon tumor GW98-166	21940	7.3	14.60	colon tumor	-1.521917808
colon normal GW98-178	22080	0	0.00	colon normal	
colon tumor GW98-177	22060	2.57	5.14	colon tumor	5.14
colon normal GW98-561	23514	0	0.00	colon normal	
colon tumor GW98-560	23513	0	0.00	colon tumor	0
colon normal GW98-894	24691	2.71	5.42	colon normal	
colon tumor GW98-893	24690	8.51	17.02	colon tumor	3.140221402
lung normal GW98-3	20742	1.78	3.56	lung normal	
lung tumor GW98-2	20741	0	0.00	lung tumor	-3.56
lung normal GW97-179	20677	3.18	6.36	lung normal	
lung tumor GW97-178	20676	2.64	5.28	lung tumor	-1.204545455
lung normal GW98-165	21922	6.46	12.92	lung normal	
lung tumor GW98-164	21921	19.99	39.98	lung tumor	3.094427245
lung normal GW98-282	22584	31.56	63.12	lung normal	

lung tumor GW98-281	22583	7.47	14.94	lung tumor	-4.224899598
breast normal GW00-392	28750	5.68	5.68	breast normal	
breast tumor GW00-391	28746	2.87	5.74	breast tumor	1.01056338
breast normal GW00-413	28798	1.66	1.66	breast normal	
breast tumor GW00-412	28797	1.99	3.98	breast tumor	2.397590361
breast normal GW00-235:238	27592-95	0	0.00	breast normal	
breast tumor GW00-231:234	27588-91	2.19	2.19	breast tumor	2.19
breast normal GW98-621	23656	4.72	9.44	breast normal	
breast tumor GW98-620	23655	0	0.00	breast tumor	-9.44
brain normal BB99-542	25507	28.9	57.80	brain normal	
brain normal BB99-406	25509	24.84	49.68	brain normal	
brain normal BB99-904	25546	6.92	13.84	brain normal	
brain stage 5 ALZ BB99-874	25502	23.65	47.30	brain stage 5 ALZ	1.169634026
brain stage 5 ALZ BB99-887	25503	28.68	57.36	brain stage 5 ALZ	1.418397626
brain stage 5 ALZ BB99-862	25504	18.18	36.36	brain stage 5 ALZ	-1.112211221
brain stage 5 ALZ BB99-927	25542	14.18	28.36	brain stage 5 ALZ	-1.425952045
CT lung KC	normal	29.45	58.90	CT lung	
lung 26 KC	normal	2.47	2.47	lung 26	
lung 27 KC	normal	0	0.00	lung 27	
lung 24 KC	COPD	0	0.00	lung 24	-15.3425
lung 28 KC	COPD	0.3	0.30	lung 28	-51.14166667
lung 23 KC	COPD	0	0.00	lung 23	-15.3425
lung 25 KC	COPD	0	0.00	lung 25	
asthmatic lung ODO3112	29321	3.24	3.24	asthmatic lung	-4.735339506
asthmatic lung ODO3433	29323	88.32	176.64	asthmatic lung	11.51311716
asthmatic lung ODO3397	29322	55.65	111.30	asthmatic lung	7.254358807
asthmatic lung ODO4928	29325	50.64	101.28	asthmatic lung	6.601270979
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		0	0.00	endo VEGF	0
endo bFGF KC		0	0.00	endo bFGF	0
heart Clontech	normal	15.26	30.52	heart	
heart (T-1) ischemic	29417	0	0.00	heart T-1	-30.52
heart (T-14) non-obstructive DCM	29422	3.69	7.38	heart T-14	-4.135501355
heart (T-3399) DCM	29426	0	0.00	heart T-3399	-30.52
adenoid GW99-269	26162	0	0.00	adenoid	
tonsil GW98-280	22582	3.65	7.30	tonsil	
T cells PC00314	28453	167.51	335.02	T cells	
PBMNC KC		2.5	2.50	PBMNC	

monocyte KC		2.37	4.74	monocyte	
B cells PC00665	28455	0	0.00	B cells	
dendritic cells 28441		0	0.00	dendritic cells	
neutrophils	28440	1576.76	1576.76	neutrophils	
eosinophils	28446	755.1	1510.20	eosinophils	
BM unstim KC		14.87	14.87	BM unstim	
BM stim KC		45.45	45.45	BM stim	3.056489576
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		7.48	18.70	chondrocytes	
OA Synovium IP12/01	29462	17.79	17.79	OA Synovium	
OA Synovium NP10/01	29461	14.09	28.18	OA Synovium	
OA Synovium NP57/00	28464	11.97	23.94	OA Synovium	
RA Synovium NP03/01	28466	6.84	13.68	RA Synovium	
RA Synovium NP71/00	28467	22.88	45.76	RA Synovium	
RA Synovium NP45/00	28475	1.64	3.28	RA Synovium	
OA bone (biobank)	29217	370.22	370.22	OA bone (biobank)	
OA bone Sample 1	J. Emory	3.21	6.42	OA bone	
OA bone Sample 2	J. Emory	311.65	623.30	OA bone	
Cartilage (pool)	Normal	32.23	64.46	Cartilage (pool)	
Cartilage (pool)	OA	2.87	5.74	Cartilage (pool)	-11.22996516
PBL unifected	28441	4.18	8.36	PBL unifected	
PBL HIV IIIB	28442	0	0.00	PBL HIV IIIB	-8.36
MRC5 uninfected (100%)	29158	4.4	8.80	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	11.46	22.92	MRC5 HSV strain F	2.604545455
W12 cells	29179	0	0.00	W12 cells	
Keratinocytes	29180	0	0.00	Keratinocytes	

Gene Name sbg425649KINASEa

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	-1.52
colon tumor	5.14
colon tumor	0.00
colon tumor	3.14

lung tumor	-3.56
lung tumor	-1.20
lung tumor	3.09
lung tumor	-4.22
breast tumor	1.01
breast tumor	2.40
breast tumor	2.19
breast tumor	-9.44
brain stage 5 ALZ	1.17
brain stage 5 ALZ	1.42
brain stage 5 ALZ	-1.11
brain stage 5 ALZ	-1.43
lung 24	-15.34
lung 28	-51.14
lung 23	-15.34
asthmatic lung	-4.74
asthmatic lung	11.51
asthmatic lung	7.25
asthmatic lung	6.60
endo VEGF	0.00
endo bFGF	0.00
heart T-1	-30.52
heart T-14	-4.14
heart T-3399	-30.52
BM stim	3.06
osteo undif	0.00
Cartilage (pool)	-11.23
PBL HIV IIIB	-8.36
MRC5 HSV strain F	2.60

Gene Name sbg419582PROTOCADHERIN
Brain specific expression. No correlation with Alzheimer's disease. Low expression in RA and OA synovium but no corroborating expression in immune cells. Slightly upregulated in heart disease. Overexpressed in lung (1/4) and breast (1/4) tumors.

Sample sbg419582PROTOCADHERIN	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/ 50 ng total RNA**
Subcutaneous Adipocytes Zenbio	18.18	23.43	20.81	3.06	16.34	339.95
Subcutaneous Adipose Zenbio	0.11	0.33	0.22	0.96	52.36	11.52
Adrenal Gland Clontech	1.8	1.06	1.43	0.61	81.97	117.21
Whole Brain Clontech	10913.92	10314.42	10614.17	7.24	6.91	73302.28
Fetal Brain Clontech	0.31	4.68	2.50	0.48	103.95	259.36
Cerebellum Clontech	0.1	4.58	2.34	2.17	23.04	53.92
Cervix	0.22	1.22	0.72	2.42	20.66	14.88
Colon	0.31	13.73	7.02	2.71	18.45	129.52
Endometrium	0.1	0.58	0.34	0.73	68.21	23.19
Esophagus	2.21	1.96	2.09	1.37	36.50	76.09
Heart Clontech	0.32	0	0.16	1.32	37.88	6.06

Hypothalamus	0.15	1.2	0.68	0.32	155.28	104.81
Ileum	2.77	1.03	1.90	2.58	19.38	36.82
Jejunum	0.26	1.18	0.72	6.60	7.58	5.45
Kidney	1.99	0.28	1.14	2.12	23.58	26.77
Liver	7.59	12.42	10.01	1.50	33.33	333.50
Fetal Liver Clontech	18.75	11.04	14.90	10.40	4.81	71.61
Lung	7.19	0.71	3.95	2.57	19.46	76.85
Mammary Gland Clontech	88.14	97.88	93.01	13.00	3.85	357.73
Myometrium	0.51	4.8	2.66	2.34	21.37	56.73
Omentum	7.52	2.19	4.86	3.94	12.69	61.61
Ovary	13.46	4.84	9.15	4.34	11.52	105.41
Pancreas	0.49	1.02	0.76	0.81	61.80	46.66
Head of Pancreas	0.29	0.15	0.22	1.57	31.85	7.01
Parotid Gland	6.09	6.19	6.14	5.48	9.12	56.02
Placenta Clontech	10.67	2.35	6.51	5.26	9.51	61.88
Prostate	2.02	3.59	2.81	3.00	16.67	46.75
Rectum	0.54	7.25	3.90	1.23	40.65	158.33
Salivary Gland Clontech	20.51	13.73	17.12	7.31	6.84	117.10
Skeletal Muscle Clontech	1.06	0.79	0.93	1.26	39.68	36.71
Skin	13.09	0.6	6.85	1.21	41.32	282.85
Small Intestine Clontech	0.11	2.47	1.29	0.98	51.07	65.88
Spleen	1.05	11	6.03	4.92	10.16	61.23
Stomach	0.95	1.3	1.13	2.73	18.32	20.60
Testis Clontech	2.82	3.19	3.01	0.57	87.87	264.06
Thymus Clontech	117.82	118.81	118.32	9.89	5.06	598.15
Thyroid	2.34	2.29	2.32	2.77	18.05	41.79
Trachea Clontech	8.72	9.37	9.05	9.71	5.15	46.58
Urinary Bladder	14.23	16.82	15.53	5.47	9.14	141.91
Uterus	1.49	27.26	14.38	5.34	9.36	134.60

Sample sbg419582PROTOCADHERIN	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	464.48	928.96	colon normal	
colon tumor GW98-166	21940	84.22	168.44	colon tumor	-5.515079554
colon normal GW98-178	22080	32.8	65.60	colon normal	
colon tumor GW98-177	22060	44.71	89.42	colon tumor	1.363109756
colon normal GW98-561	23514	135.5	271.00	colon normal	
colon tumor GW98-560	23513	78.51	157.02	colon tumor	-1.72589479
colon normal GW98-894	24691	454.16	908.32	colon normal	
colon tumor GW98-893	24690	51.37	102.74	colon tumor	-8.840957757
lung normal GW98-3	20742	60.35	120.70	lung normal	
lung tumor GW98-2	20741	101.98	203.96	lung tumor	1.689809445

lung normal GW97-179	20677	264	528.00	lung normal	
lung tumor GW97-178	20676	78.49	156.98	lung tumor	-3.363485794
lung normal GW98-165	21922	88.19	176.38	lung normal	
lung tumor GW98-164	21921	7554.58	15109.16	lung tumor	85.66254677
lung normal GW98-282	22584	344.2	688.40	lung normal	
lung tumor GW98-281	22583	45.51	91.02	lung tumor	-7.563172929
breast normal GW00-392	28750	132.43	132.43	breast normal	
breast tumor GW00-391	28746	98.14	196.28	breast tumor	1.482141509
breast normal GW00-413	28798	154.37	154.37	breast normal	
breast tumor GW00-412	28797	1289.09	2578.18	breast tumor	16.70130207
breast normal GW00-235:238	27592-95	18.63	18.63	breast normal	
breast tumor GW00-231:234	27588-91	133.52	133.52	breast tumor	7.166935051
breast normal GW98-621	23656	1334.91	2669.82	breast normal	
breast tumor GW98-620	23655	212.39	424.78	breast tumor	-6.285182918
brain normal BB99-542	25507	6816.47	13632.94	brain normal	
brain normal BB99-406	25509	1984.48	3968.96	brain normal	
brain normal BB99-904	25546	2805.82	5611.64	brain normal	
brain stage 5 ALZ BB99-874	25502	467.59	935.18	brain stage 5 ALZ	-8.274178946
brain stage 5 ALZ BB99-887	25503	3104.22	6208.44	brain stage 5 ALZ	-1.24634315
brain stage 5 ALZ BB99-862	25504	1889.81	3779.62	brain stage 5 ALZ	-2.047255191
brain stage 5 ALZ BB99-927	25542	2902.29	5804.58	brain stage 5 ALZ	-1.333058837
CT lung KC	normal	103.32	206.64	CT lung	
lung 26 KC	normal	1.13	1.13	lung 26	
lung 27 KC	normal	1.51	1.51	lung 27	
lung 24 KC	COPD	1.47	1.47	lung 24	-35.82312925
lung 28 KC	COPD	0	0.00	lung 28	-52.66
lung 23 KC	COPD	1.91	1.91	lung 23	-27.57068063
lung 25 KC	COPD	1.36	1.36	lung 25	
asthmatic lung ODO3112	29321	2.68	2.68	asthmatic lung	-19.64925373
asthmatic lung ODO3433	29323	3.25	6.50	asthmatic lung	-8.101538462
asthmatic lung ODO3397	29322	26.23	52.46	asthmatic lung	-1.003812429
asthmatic lung ODO4928	29325	7.15	14.30	asthmatic lung	-3.682517483
endo cells KC	control	15.9	15.90	endo cells	
endo VEGF KC		8.26	8.26	endo VEGF	-1.924939467
endo bFGF KC		2.01	2.01	endo bFGF	-7.910447761
heart Clontech	normal	7.9	15.80	heart	
heart (T-1) ischemic	29417	67.47	134.94	heart T-1	8.540506329
heart (T-14) non-obstructive DCM	29422	106.83	213.66	heart T-14	13.52278481

heart (T-3399) DCM	29426	425.28	850.56	heart T-3399	53.83291139
adenoid GW99-269	26162	15.98	31.96	adenoid	
tonsil GW98-280	22582	17.95	35.90	tonsil	
T cells PC00314	28453	3.18	6.36	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		0.81	1.62	monocyte	
B cells PC00665	28455	2.74	5.48	B cells	
dendritic cells 28441		0	0.00	dendritic cells	
neutrophils	28440	0	0.00	neutrophils	
eosinophils	28446	0	0.00	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		0	0.00	BM stim	0
osteo dif KC		2.34	2.34	osteo dif	
osteo undif KC		0	0.00	osteo undif	-2.34
chondrocytes		145.14	362.85	chondrocytes	
OA Synovium IP12/01	29462	320.78	320.78	OA Synovium	
OA Synovium NP10/01	29461	396.85	793.70	OA Synovium	
OA Synovium NP57/00	28464	329.87	659.74	OA Synovium	
RA Synovium NP03/01	28466	103.85	207.70	RA Synovium	
RA Synovium NP71/00	28467	617.72	1235.44	RA Synovium	
RA Synovium NP45/00	28475	63.13	126.26	RA Synovium	
OA bone (biobank)	29217	3.19	3.19	OA bone (biobank)	
OA bone Sample 1	J. Emory	126.87	253.74	OA bone	
OA bone Sample 2	J. Emory	44.76	89.52	OA bone	
Cartilage (pool)	Normal	502.66	1005.32	Cartilage (pool)	
Cartilage (pool)	OA	206.76	413.52	Cartilage (pool)	-2.431127878
PBL unifected	28441	0	0.00	PBL unifected	
PBL HIV IIIB	28442	0	0.00	PBL HIV IIIB	0
MRC5 uninfected (100%)	29158	0	0.00	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	17.73	35.46	MRC5 HSV strain F	35.46
W12 cells	29179	0.62	1.24	W12 cells	
Keratinocytes	29180	22.63	45.26	Keratinocytes	

Gene Name sbg419582PROTOCADHERIN

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	-5.52
colon tumor	1.36
colon tumor	-1.73
colon tumor	-8.84
lung tumor	1.69
lung tumor	-3.36
lung tumor	85.66
lung tumor	-7.56
breast tumor	1.48
breast tumor	16.70
breast tumor	7.17
breast tumor	-6.29
brain stage 5 ALZ	-8.27
brain stage 5 ALZ	-1.25
brain stage 5 ALZ	-2.05
brain stage 5 ALZ	-1.33
lung 24	-35.82
lung 28	-52.66
lung 23	-27.57
asthmatic lung	-19.65
asthmatic lung	-8.10
asthmatic lung	-1.00
asthmatic lung	-3.68
endo VEGF	-1.92
endo bFGF	-7.91
heart T-1	8.54
heart T-14	13.52
heart T-3399	53.83
BM stim	0.00
osteo undif	-2.34
Cartilage (pool)	-2.43
PBL HIV IIIB	0.00
MRC5 HSV strain F	35.46

Gene Name sbg453915TECTORINa

Very low expression overall. Expression in female reproductive tissues suggests a protein that may be secreted by these tissue types.

Sample sbg453915TECTORINa	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	2.70	5.41	4.06	3.06	16.34	66.26
Subcutaneous Adipose	0.00	0.00	0.00	0.96	52.36	0.00

Zenbio						
Adrenal Gland Clontech	3.75	5.67	4.71	0.61	81.97	386.07
Whole Brain Clontech	22.57	27.88	25.23	7.24	6.91	174.21
Fetal Brain Clontech	2.42	1.80	2.11	0.48	103.95	219.33
Cerebellum Clontech	0.00	1.93	0.97	2.17	23.04	22.24
Cervix	2.90	2.10	2.50	2.42	20.66	51.65
Colon	11.19	2.68	6.94	2.71	18.45	127.95
Endometrium	4.79	19.31	12.05	0.73	68.21	821.96
Esophagus	2.06	2.93	2.50	1.37	36.50	91.06
Heart Clontech	5.42	7.31	6.37	1.32	37.88	241.10
Hypothalamus	0.00	3.70	1.85	0.32	155.28	287.27
Ileum	3.72	18.75	11.24	2.58	19.38	217.73
Jejunum	28.49	49.80	39.15	6.60	7.58	296.55
Kidney	2.12	4.37	3.25	2.12	23.58	76.53
Liver	15.74	39.80	27.77	1.50	33.33	925.67
Fetal Liver Clontech	27.96	26.14	27.05	10.40	4.81	130.05
Lung	0.00	2.37	1.19	2.57	19.46	23.05
Mammary Gland Clontech	19.68	19.22	19.45	13.00	3.85	74.81
Myometrium	3.40	1.71	2.56	2.34	21.37	54.59
Omentum	14.33	138.99	76.66	3.94	12.69	972.84
Ovary	46.55	37.80	42.18	4.34	11.52	485.89
Pancreas	4.26	2.19	3.23	0.81	61.80	199.32
Head of Pancreas	1.93	1.52	1.73	1.57	31.85	54.94
Parotid Gland	4.04	5.93	4.99	5.48	9.12	45.48
Placenta Clontech	3.69	15.48	9.59	5.26	9.51	91.11
Prostate	7.94	28.75	18.35	3.00	16.67	305.75
Rectum	11.09	3.41	7.25	1.23	40.65	294.72
Salivary Gland Clontech	0.00	1.45	0.73	7.31	6.84	4.96
Skeletal Muscle Clontech	4.76	0.00	2.38	1.26	39.68	94.44
Skin	0.00	1.39	0.70	1.21	41.32	28.72
Small Intestine Clontech	2.20	1.41	1.81	0.98	51.07	92.19
Spleen	7.15	8.12	7.64	4.92	10.16	77.59
Stomach	1.98	0.00	0.99	2.73	18.32	18.13
Testis Clontech	6.83	2.61	4.72	0.57	87.87	414.76
Thymus Clontech	0.00	0.00	0.00	9.89	5.06	0.00
Thyroid	2.38	1.88	2.13	2.77	18.05	38.45
Trachea Clontech	1.71	9.25	5.48	9.71	5.15	28.22
Urinary Bladder	3.72	8.22	5.97	5.47	9.14	54.57
Uterus	74.31	73.54	73.93	5.34	9.36	692.18

Sample sbg453915TECTORINa	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	131.15	262.30	colon normal	
colon tumor GW98-166	21940	85.76	171.52	colon tumor	-1.529267724
colon normal GW98-178	22080	1.82	3.64	colon normal	
colon tumor GW98-177	22060	10.14	20.28	colon tumor	5.571428571
colon normal GW98-561	23514	14.25	28.50	colon normal	
colon tumor GW98-560	23513	9.89	19.78	colon tumor	-1.440849343
colon normal GW98-894	24691	32.05	64.10	colon normal	
colon tumor GW98-893	24690	53.06	106.12	colon tumor	1.655538222
lung normal GW98-3	20742	6.9	13.80	lung normal	
lung tumor GW98-2	20741	0.81	1.62	lung tumor	-8.518518519
lung normal GW97-179	20677	1.19	2.38	lung normal	
lung tumor GW97-178	20676	0	0.00	lung tumor	-2.38
lung normal GW98-165	21922	0.91	1.82	lung normal	
lung tumor GW98-164	21921	5.99	11.98	lung tumor	6.582417582
lung normal GW98-282	22584	5.93	11.86	lung normal	
lung tumor GW98-281	22583	1.54	3.08	lung tumor	-3.850649351
breast normal GW00-392	28750	6.88	6.88	breast normal	
breast tumor GW00-391	28746	4.24	8.48	breast tumor	1.23255814
breast normal GW00-413	28798	0	0.00	breast normal	
breast tumor GW00-412	28797	13.96	27.92	breast tumor	27.92
breast normal GW00-235:238	27592-95	14.42	14.42	breast normal	
breast tumor GW00-231:234	27588-91	0	0.00	breast tumor	-14.42
breast normal GW98-621	23656	5.81	11.62	breast normal	
breast tumor GW98-620	23655	0	0.00	breast tumor	-11.62
brain normal BB99-542	25507	20.59	41.18	brain normal	
brain normal BB99-406	25509	15.98	31.96	brain normal	
brain normal BB99-904	25546	2.38	4.76	brain normal	
brain stage 5 ALZ BB99-874	25502	25.45	50.90	brain stage 5 ALZ	1.960205392
brain stage 5 ALZ BB99-887	25503	35.78	71.56	brain stage 5 ALZ	2.755840822
brain stage 5 ALZ BB99-862	25504	13.83	27.66	brain stage 5 ALZ	1.06521181
brain stage 5 ALZ BB99-927	25542	21.67	43.34	brain stage 5 ALZ	1.669062901
CT lung KC	normal	6.52	13.04	CT lung	
lung 26 KC	normal	2.1	2.10	lung 26	
lung 27 KC	normal	0.84	0.84	lung 27	
lung 24 KC	COPD	1.25	1.25	lung 24	-3.432
lung 28 KC	COPD	0	0.00	lung 28	-4.29
lung 23 KC	COPD	1.16	1.16	lung 23	-3.698275862

lung 25 KC	COPD	1.18	1.18	lung 25	
asthmatic lung ODO3112	29321	4.9	4.90	asthmatic lung	1.142191142
asthmatic lung ODO3433	29323	0.83	1.66	asthmatic lung	-2.584337349
asthmatic lung ODO3397	29322	2.46	4.92	asthmatic lung	1.146853147
asthmatic lung ODO4928	29325	6	12.00	asthmatic lung	2.797202797
endo cells KC	control	2.52	2.52	endo cells	
endo VEGF KC		1.28	1.28	endo VEGF	-1.96875
endo bFGF KC		0	0.00	endo bFGF	-2.52
heart Clontech	normal	0	0.00	heart	
heart (T-1) ischemic	29417	3.58	7.16	heart T-1	7.16
heart (T-14) non-obstructive DCM	29422	0	0.00	heart T-14	0
heart (T-3399)DCM	29426	0	0.00	heart T-3399	0
adenoid GW99-269	26162	2.29	4.58	adenoid	
tonsil GW98-280	22582	1.85	3.70	tonsil	
T cells PC00314	28453	4.29	8.58	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		3.39	6.78	monocyte	
B cells PC00665	28455	6.04	12.08	B cells	
dendritic cells 28441		0.83	1.66	dendritic cells	
neutrophils	28440	34.69	34.69	neutrophils	
eosinophils	28446	2.86	5.72	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		12.8	12.80	BM stim	12.8
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		4.78	11.95	chondrocytes	
OA Synovium IP12/01	29462	18.31	18.31	OA Synovium	
OA Synovium NP10/01	29461	0	0.00	OA Synovium	
OA Synovium NP57/00	28464	11.46	22.92	OA Synovium	
RA Synovium NP03/01	28466	0.87	1.74	RA Synovium	
RA Synovium NP71/00	28467	26.95	53.90	RA Synovium	
RA Synovium NP45/00	28475	18.91	37.82	RA Synovium	
OA bone (biobank)	29217	0	0.00	OA bone (biobank)	
OA bone Sample 1	J. Emory	8.66	17.32	OA bone	
OA bone Sample 2	J. Emory	7.8	15.60	OA bone	
Cartilage (pool)	Normal	16.93	33.86	Cartilage (pool)	
Cartilage (pool)	OA	6.39	12.78	Cartilage (pool)	-2.649452269

PBL unifected	28441	0	0.00	PBL unifected	
PBL HIV IIIB	28442	1.15	2.30	PBL HIV IIIB	2.3
MRC5 uninfected (100%)	29158	0	0.00	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	70.84	141.68	MRC5 HSV strain F	141.68
W12 cells	29179	5.59	11.18	W12 cells	
Keratinocytes	29180	0	0.00	Keratinocytes	

Gene Name sbg453915TECTORINa

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	-1.53
colon tumor	5.57
colon tumor	-1.44
colon tumor	1.66
lung tumor	-8.52
lung tumor	-2.38
lung tumor	6.58
lung tumor	-3.85
breast tumor	1.23
breast tumor	27.92
breast tumor	-14.42
breast tumor	-11.62
brain stage 5 ALZ	1.96
brain stage 5 ALZ	2.76
brain stage 5 ALZ	1.07
brain stage 5 ALZ	1.67
lung 24	-3.43
lung 28	-4.29
lung 23	-3.70
asthmatic lung	1.14
asthmatic lung	-2.58
asthmatic lung	1.15
asthmatic lung	2.80
endo VEGF	-1.97
endo bFGF	-2.52
heart T-1	7.16
heart T-14	0.00
heart T-3399	0.00
BM stim	12.80
osteo undif	0.00
Cartilage (pool)	-2.65
PBL HIV IIIB	2.30
MRC5 HSV strain F	141.68

Gene Name SBh385630.antiinflam

Some expression in adenoid, tonsils and T-cells suggesting a role in the immune system. Expression in GI tissues suggests a role in the digestive system and potential role in

diseases of the GI system such as IBD. Overexpression in lung (1/4) and colon tumors (1/4) suggesting a role in lung and colon cancer. Increased expression in ischemic and dilated heart samples indicating a role in Cardiovascular diseases that are consistent with cardiac hypertrophy. Expression in whole brain but not localized to hypothalamus, cerebellum or cortex.

Sample SBh385630.antiinflam	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	6.41	3.21	3.06	16.34	52.37
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	8.40	0.00	4.20	0.61	81.97	344.26
Whole Brain Clontech	817.17	466.76	641.97	7.24	6.91	4433.46
Fetal Brain Clontech	3.80	0.00	1.90	0.48	103.95	197.51
Cerebellum Clontech	6.66	0.00	3.33	2.17	23.04	76.73
Cervix	11.99	12.30	12.15	2.42	20.66	250.93
Colon	55.51	211.32	133.42	2.71	18.45	2461.53
Endometrium	0.00	0.00	0.00	0.73	68.21	0.00
Esophagus	11.75	30.29	21.02	1.37	36.50	767.15
Heart Clontech	0.00	0.00	0.00	1.32	37.88	0.00
Hypothalamus	0.00	0.00	0.00	0.32	155.28	0.00
Ileum	40.37	42.85	41.61	2.58	19.38	806.40
Jejunum	200.19	263.82	232.01	6.60	7.58	1757.61
Kidney	18.38	34.53	26.46	2.12	23.58	623.94
Liver	11.00	17.20	14.10	1.50	33.33	470.00
Fetal Liver Clontech	150.74	123.93	137.34	10.40	4.81	660.26
Lung	82.73	77.24	79.99	2.57	19.46	1556.13
Mammary Gland Clontech	161.37	155.19	158.28	13.00	3.85	608.77
Myometrium	5.79	9.38	7.59	2.34	21.37	162.07
Omentum	36.14	46.80	41.47	3.94	12.69	526.27
Ovary	59.25	44.29	51.77	4.34	11.52	596.43
Pancreas	6.29	6.70	6.50	0.81	61.80	401.42
Head of Pancreas	0.00	26.25	13.13	1.57	31.85	417.99
Parotid Gland	8.77	52.96	30.87	5.48	9.12	281.61
Placenta Clontech	4.11	0.00	2.06	5.26	9.51	19.53
Prostate	100.91	49.99	75.45	3.00	16.67	1257.50
Rectum	180.24	305.61	242.93	1.23	40.65	9875.00
Salivary Gland Clontech	49.36	70.01	59.69	7.31	6.84	408.24
Skeletal Muscle Clontech	0.00	0.00	0.00	1.26	39.68	0.00
Skin	18.00	3.22	10.61	1.21	41.32	438.43
Small Intestine Clontech	3.90	2.55	3.23	0.98	51.07	164.71

Spleen	9.67	5.60	7.64	4.92	10.16	77.59
Stomach	32.34	83.60	57.97	2.73	18.32	1061.72
Testis Clontech	3.53	0.00	1.77	0.57	87.87	155.10
Thymus Clontech	73.66	60.02	66.84	9.89	5.06	337.92
Thyroid	15.87	12.31	14.09	2.77	18.05	254.33
Trachea Clontech	98.68	187.11	142.90	9.71	5.15	735.81
Urinary Bladder	118.92	101.91	110.42	5.47	9.14	1009.28
Uterus	9.03	24.21	16.62	5.34	9.36	155.62

Sample SBh385630.antiinflam	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	6479.77	12959.54	colon normal	
colon tumor GW98-166	21940	7824.02	15648.04	colon tumor	1.207453351
colon normal GW98-178	22080	343.81	687.62	colon normal	
colon tumor GW98-177	22060	3011.93	6023.86	colon tumor	8.760449085
colon normal GW98-561	23514	5457.38	10914.76	colon normal	
colon tumor GW98-560	23513	4017.14	8034.28	colon tumor	-1.358523726
colon normal GW98-894	24691	14903.68	29807.36	colon normal	
colon tumor GW98-893	24690	4814.19	9628.38	colon tumor	-3.095781429
lung normal GW98-3	20742	3731.84	7463.68	lung normal	
lung tumor GW98-2	20741	719.6	1439.20	lung tumor	-5.185992218
lung normal GW97-179	20677	1090.56	2181.12	lung normal	
lung tumor GW97-178	20676	6187.22	12374.44	lung tumor	5.673433832
lung normal GW98-165	21922	8416.82	16833.64	lung normal	
lung tumor GW98-164	21921	4405.14	8810.28	lung tumor	-1.910681613
lung normal GW98-282	22584	2033.26	4066.52	lung normal	
lung tumor GW98-281	22583	1785.69	3571.38	lung tumor	-1.138641086
breast normal GW00-392	28750	1583.49	1583.49	breast normal	
breast tumor GW00-391	28746	1334.89	2669.78	breast tumor	1.686010016
breast normal GW00-413	28798	1225.92	1225.92	breast normal	
breast tumor GW00-412	28797	1213.71	2427.42	breast tumor	1.980080266
breast normal GW00-235:238	27592-95	862.26	862.26	breast normal	
breast tumor GW00-231:234	27588-91	1766.08	1766.08	breast tumor	2.048198919
breast normal GW98-621	23656	1420.57	2841.14	breast normal	
breast tumor GW98-620	23655	760.05	1520.10	breast tumor	-1.869048089
brain normal BB99-542	25507	679.48	1358.96	brain normal	
brain normal BB99-406	25509	423.69	847.38	brain normal	
brain normal BB99-904	25546	401.34	802.68	brain normal	
brain stage 5 ALZ BB99-874	25502	264.51	529.02	brain stage 5 ALZ	-1.895971167
brain stage 5 ALZ BB99-887	25503	648.88	1297.76	brain stage 5 ALZ	1.293869765

brain stage 5 ALZ BB99-862	25504	234.97	469.94	brain stage 5 ALZ	-2.134329205
brain stage 5 ALZ BB99-927	25542	404.55	809.10	brain stage 5 ALZ	-1.239657232
CT lung KC	normal	6620.85	13241.70	CT lung	
lung 26 KC	normal	320.43	320.43	lung 26	
lung 27 KC	normal	164.59	164.59	lung 27	
lung 24 KC	COPD	141.57	141.57	lung 24	-25.25392032
lung 28 KC	COPD	323.8	323.80	lung 28	-11.04137585
lung 23 KC	COPD	363.35	363.35	lung 23	-9.839541764
lung 25 KC	COPD	574.07	574.07	lung 25	
asthmatic lung ODO3112	29321	6073.99	6073.99	asthmatic lung	1.698924325
asthmatic lung ODO3433	29323	4568.41	9136.82	asthmatic lung	2.555612662
asthmatic lung ODO3397	29322	17389.11	34778.22	asthmatic lung	9.727636026
asthmatic lung ODO4928	29325	4719.27	9438.54	asthmatic lung	2.640005203
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		0	0.00	endo VEGF	0
endo bFGF KC		0	0.00	endo bFGF	0
heart Clontech	normal	10.63	21.26	heart	
heart (T-1) ischemic	29417	599.01	1198.02	heart T-1	56.3508937
heart (T-14) non-obstructive DCM	29422	666.41	1332.82	heart T-14	62.69143932
heart (T-3399) DCM	29426	142.85	285.70	heart T-3399	13.43838194
adenoid GW99-269	26162	1138	2276.00	adenoid	
tonsil GW98-280	22582	561.57	1123.14	tonsil	
T cells PC00314	28453	736.27	1472.54	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		30.38	60.76	monocyte	
B cells PC00665	28455	204.15	408.30	B cells	
dendritic cells 28441		57.66	115.32	dendritic cells	
neutrophils	28440	13.3	13.30	neutrophils	
eosinophils	28446	5.71	11.42	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		50.38	50.38	BM stim	50.38
osteo dif KC		8.62	8.62	osteo dif	
osteo undif KC		0	0.00	osteo undif	-8.62
chondrocytes		14.98	37.45	chondrocytes	
OA Synovium IP12/01	29462	134.63	134.63	OA Synovium	
OA Synovium NP10/01	29461	73.89	147.78	OA Synovium	
OA Synovium NP57/00	28464	106.98	213.96	OA Synovium	
RA Synovium NP03/01	28466	26.59	53.18	RA Synovium	
RA Synovium NP71/00	28467	60.88	121.76	RA	

				Synovium	
RA Synovium NP45/00	28475	60.81	121.62	RA Synovium	
OA bone (biobank)	29217	98.18	98.18	OA bone (biobank)	
OA bone Sample 1	J. Emory	78.3	156.60	OA bone	
OA bone Sample 2	J. Emory	107.7	215.40	OA bone	
Cartilage (pool)	Normal	72.21	144.42	Cartilage (pool)	
Cartilage (pool)	OA	48.61	97.22	Cartilage (pool)	-1.485496811
PBL unifected	28441	30.22	60.44	PBL unifected	
PBL HIV IIIB	28442	21.89	43.78	PBL HIV IIIB	-1.380539059
MRC5 uninfected (100%)	29158	10.74	21.48	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	171.23	342.46	MRC5 HSV strain F	15.94320298
W12 cells	29179	1143.85	2287.70	W12 cells	
Keratinocytes	29180	388.06	776.12	Keratinocytes	

Gene Name SBh385630.antiinflam

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	1.21
colon tumor	8.76
colon tumor	-1.36
colon tumor	-3.10
lung tumor	-5.19
lung tumor	5.67
lung tumor	-1.91
lung tumor	-1.14
breast tumor	1.69
breast tumor	1.98
breast tumor	2.05
breast tumor	-1.87
brain stage 5 ALZ	-1.90
brain stage 5 ALZ	1.29
brain stage 5 ALZ	-2.13
brain stage 5 ALZ	-1.24
lung 24	-25.25
lung 28	-11.04
lung 23	-9.84
asthmatic lung	1.70
asthmatic lung	2.56
asthmatic lung	9.73
asthmatic lung	2.64
endo VEGF	0.00
endo bFGF	0.00
heart T-1	56.35

heart T-14	62.69
heart T-3399	13.44
BM stim	50.38
osteo undif	-8.62
Cartilage (pool)	-1.49
PBL HIV IIIB	-1.38
MRC5 HSV strain F	15.94

Gene Name sbg471005nAChR

Expressed in immune cells with corroborating expression in OA and RA synovium suggesting a role in this disease.

High expression in whole brain but not present in cortex, cerebellum, or hypothalamus suggesting localized brain expression.

Sample sbg471005nAChR	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/50 ng total RNA**
Subcutaneous Adipocytes Zenbio	32.42	2.90	17.66	3.06	16.34	288.56
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	0.00	0.00	0.00	0.61	81.97	0.00
Whole Brain Clontech	1606.00	1058.07	1332.04	7.24	6.91	9199.14
Fetal Brain Clontech	0.00	6.34	3.17	0.48	103.95	329.52
Cerebellum Clontech	10.65	0.00	5.33	2.17	23.04	122.70
Cervix	0.00	0.00	0.00	2.42	20.66	0.00
Colon	0.00	0.00	0.00	2.71	18.45	0.00
Endometrium	0.00	0.00	0.00	0.73	68.21	0.00
Esophagus	0.00	2.52	1.26	1.37	36.50	45.99
Heart Clontech	4.05	0.00	2.03	1.32	37.88	76.70
Hypothalamus	2.24	0.00	1.12	0.32	155.28	173.91
Ileum	0.00	0.00	0.00	2.58	19.38	0.00
Jejunum	20.32	41.44	30.88	6.60	7.58	233.94
Kidney	14.56	0.00	7.28	2.12	23.58	171.70
Liver	3.55	10.72	7.14	1.50	33.33	237.83
Fetal Liver Clontech	127.95	116.81	122.38	10.40	4.81	588.37
Lung	12.79	0.00	6.40	2.57	19.46	124.42
Mammary Gland Clontech	30.53	24.12	27.33	13.00	3.85	105.10
Myometrium	0.00	7.10	3.55	2.34	21.37	75.85
Omentum	8.15	0.00	4.08	3.94	12.69	51.71
Ovary	18.27	7.02	12.65	4.34	11.52	145.68
Pancreas	0.00	0.00	0.00	0.81	61.80	0.00
Head of Pancreas	0.00	0.00	0.00	1.57	31.85	0.00
Parotid Gland	0.00	0.00	0.00	5.48	9.12	0.00
Placenta Clontech	9.17	0.00	4.59	5.26	9.51	43.58

Prostate	0.00	1.35	0.68	3.00	16.67	11.25
Rectum	0.00	0.00	0.00	1.23	40.65	0.00
Salivary Gland Clontech	0.00	11.84	5.92	7.31	6.84	40.49
Skeletal Muscle Clontech	6.09	7.36	6.73	1.26	39.68	266.87
Skin	0.00	0.00	0.00	1.21	41.32	0.00
Small Intestine Clontech	0.00	0.00	0.00	0.98	51.07	0.00
Spleen	5.20	7.36	6.28	4.92	10.16	63.82
Stomach	12.85	6.38	9.62	2.73	18.32	176.10
Testis Clontech	0.00	2.25	1.13	0.57	87.87	98.86
Thymus Clontech	177.85	168.23	173.04	9.89	5.06	874.82
Thyroid	6.44	0.00	3.22	2.77	18.05	58.12
Trachea Clontech	5.07	0.00	2.54	9.71	5.15	13.05
Urinary Bladder	0.00	0.00	0.00	5.47	9.14	0.00
Uterus	29.20	10.39	19.80	5.34	9.36	185.35

Sample sbg471005nAChR	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	1530.09	3060.18	colon normal	
colon tumor GW98-166	21940	617.15	1234.30	colon tumor	-2.479283805
colon normal GW98-178	22080	406.03	812.06	colon normal	
colon tumor GW98-177	22060	1231.53	2463.06	colon tumor	3.033101002
colon normal GW98-561	23514	844.37	1688.74	colon normal	
colon tumor GW98-560	23513	633.99	1267.98	colon tumor	-1.331834887
colon normal GW98-894	24691	1130.51	2261.02	colon normal	
colon tumor GW98-893	24690	721.29	1442.58	colon tumor	-1.567344619
lung normal GW98-3	20742	2433.65	4867.30	lung normal	
lung tumor GW98-2	20741	334.04	668.08	lung tumor	-7.28550473_
lung normal GW97-179	20677	823.51	1647.02	lung normal	
lung tumor GW97-178	20676	1492	2984.00	lung tumor	1.811756991
lung normal GW98-165	21922	829.65	1659.30	lung normal	
lung tumor GW98-164	21921	595.31	1190.62	lung tumor	-1.393643648
lung normal GW98-282	22584	357.69	715.38	lung normal	
lung tumor GW98-281	22583	256.76	513.52	lung tumor	-1.393090824
breast normal GW00-392	28750	357.44	357.44	breast normal	
breast tumor GW00-391	28746	280.98	561.96	breast tumor	1.572179946
breast normal GW00-413	28798	286.18	286.18	breast normal	
breast tumor GW00-412	28797	195.5	391.00	breast tumor	1.366272975
breast normal GW00-235:238	27592-95	161.68	161.68	breast normal	
breast tumor GW00-231:234	27588-91	217.83	217.83	breast tumor	1.347290945
breast normal GW98-621	23656	531.53	1063.06	breast normal	

breast tumor GW98-620	23655	556.17	1112.34	breast tumor	1.046356744
brain normal BB99-542	25507	143.72	287.44	brain normal	
brain normal BB99-406	25509	569.17	1138.34	brain normal	
brain normal BB99-904	25546	106.85	213.70	brain normal	
brain stage 5 ALZ BB99-874	25502	286.37	572.74	brain stage 5 ALZ	1.048027423
brain stage 5 ALZ BB99-887	25503	746.74	1493.48	brain stage 5 ALZ	2.732842121
brain stage 5 ALZ BB99-862	25504	382.97	765.94	brain stage 5 ALZ	1.401554151
brain stage 5 ALZ BB99-927	25542	367.49	734.98	brain stage 5 ALZ	1.344902042
CT lung KC	normal	175.41	350.82	CT lung	
lung 26 KC	normal	20.66	20.66	lung 26	
lung 27 KC	normal	13.06	13.06	lung 27	
lung 24 KC	COPD	15.89	15.89	lung 24	-6.182662052
lung 28 KC	COPD	7.34	7.34	lung 28	-13.38453678
lung 23 KC	COPD	22.3	22.30	lung 23	-4.405493274
lung 25 KC	COPD	8.43	8.43	lung 25	
asthmatic lung ODO3112	29321	264.47	264.47	asthmatic lung	2.692012113
asthmatic lung ODO3433	29323	442.3	884.60	asthmatic lung	9.004249688
asthmatic lung ODO3397	29322	670.04	1340.08	asthmatic lung	13.64053236
asthmatic lung ODO4928	29325	414.13	828.26	asthmatic lung	8.430770797
endo cells KC	control	66.94	66.94	endo cells	
endo VEGF KC		18.49	18.49	endo VEGF	-3.620335316
endo bFGF KC		15.93	15.93	endo bFGF	-4.202134338
heart Clontech	normal	180.76	361.52	heart	
heart (T-1) ischemic	29417	161.9	323.80	heart T-1	-1.116491662
heart (T-14) non-obstructive DCM	29422	141.03	282.06	heart T-14	-1.281713111
heart (T-3399) DCM	29426	321.32	642.64	heart T-3399	1.777605665
adenoid GW99-269	26162	193.61	387.22	adenoid	
tonsil GW98-280	22582	625.4	1250.80	tonsil	
T cells PC00314	28453	140.44	280.88	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		0	0.00	monocyte	
B cells PC00665	28455	476.72	953.44	B cells	
dendritic cells 28441		205.79	411.58	dendritic cells	
neutrophils	28440	1366.99	1366.99	neutrophils	
eosinophils	28446	316.57	633.14	eosinophils	
BM unstim KC		29.41	29.41	BM unstim	
BM stim KC		46.03	46.03	BM stim	1.565113907
osteo dif KC		17.47	17.47	osteo dif	
osteo undif KC		1.87	1.87	osteo undif	-9.342245989
chondrocytes		735.88	1839.70	chondrocytes	

OA Synovium IP12/01	29462	686.8	686.80	OA Synovium	
OA Synovium NP10/01	29461	4887.16	9774.32	OA Synovium	
OA Synovium NP57/00	28464	721.49	1442.98	OA Synovium	
RA Synovium NP03/01	28466	383.33	766.66	RA Synovium	
RA Synovium NP71/00	28467	780.94	1561.88	RA Synovium	
RA Synovium NP45/00	28475	543.62	1087.24	RA Synovium	
OA bone (biobank)	29217	780.12	780.12	OA bone (biobank)	
OA bone Sample 1	J. Emory	361.65	723.30	OA bone	
OA bone Sample 2	J. Emory	197.57	395.14	OA bone	
Cartilage (pool)	Normal	220.7	441.40	Cartilage (pool)	
Cartilage (pool)	OA	75.52	151.04	Cartilage (pool)	-2.922404661
PBL unifected	28441	1745.81	3491.62	PBL unifected	
PBL HIV IIIB	28442	832.4	1664.80	PBL HIV IIIB	-2.097321
MRC5 uninfected (100%)	29158	147.92	295.84	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	146	292.00	MRC5 HSV strain F	-1.013150685
W12 cells	29179	304.27	608.54	W12 cells	
Keratinocytes	29180	139.44	278.88	Keratinocytes	

Gene Name sbg471005nAChR

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	-2.48
colon tumor	3.03
colon tumor	-1.33
colon tumor	-1.57
lung tumor	-7.29
lung tumor	1.81
lung tumor	-1.39
lung tumor	-1.39
breast tumor	1.57
breast tumor	1.37
breast tumor	1.35
breast tumor	1.05
brain stage 5 ALZ	1.05
brain stage 5 ALZ	2.73
brain stage 5 ALZ	1.40
brain stage 5 ALZ	1.34
lung 24	-6.18

lung 28	-13.38
lung 23	-4.41
asthmatic lung	2.69
asthmatic lung	9.00
asthmatic lung	13.64
asthmatic lung	8.43
endo VEGF	-3.62
endo bFGF	-4.20
heart T-1	-1.12
heart T-14	-1.28
heart T-3399	1.78
BM stim	1.57
osteo undif	-9.34
Cartilage (pool)	-2.92
PBL HIV IIIB	-2.10
MRC5 HSV strain F	-1.01

Gene Name sbg442445PROa

Strong expression in B-cells with expression in other immune cell types indicate function in immune system.Corroborating expression in RA and OA samples indicate role in disease. 2X increase in cells infected with HIV suggests possible marker in HIV infection. Expression in whole brain but not cortex or cerebellum suggests localized expression in brain.

Sample sbg442445PROa	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/50 ng total RNA**
Subcutaneous Adipocytes Zenbio	1.13	3.82	2.48	3.06	16.34	40.44
Subcutaneous Adipose Zenbio	0.63	0	0.32	0.96	52.36	16.49
Adrenal Gland Clontech	0.64	0.74	0.69	0.61	81.97	56.56
Whole Brain Clontech	368.87	396.51	382.69	7.24	6.91	2642.89
Fetal Brain Clontech	1.57	2.5	2.04	0.48	103.95	211.54
Cerebellum Clontech	1.63	0	0.82	2.17	23.04	18.78
Cervix	4.57	5.6	5.09	2.42	20.66	105.06
Colon	18.13	7.38	12.76	2.71	18.45	235.33
Endometrium	4.23	0	2.12	0.73	68.21	144.27
Esophagus	6.85	12.66	9.76	1.37	36.50	356.02
Heart Clontech	12.83	1.44	7.14	1.32	37.88	270.27
Hypothalamus	0.58	7.26	3.92	0.32	155.28	608.70
Ileum	22.89	6.34	14.62	2.58	19.38	283.24
Jejunum	6.67	36.71	21.69	6.60	7.58	164.32
Kidney	2.82	6.28	4.55	2.12	23.58	107.31
Liver	11.21	1.24	6.23	1.50	33.33	207.50
Fetal Liver Clontech	118	135.81	126.91	10.40	4.81	610.12
Lung	13.95	37.87	25.91	2.57	19.46	504.09
Mammary Gland Clontech	15.77	11.19	13.48	13.00	3.85	51.85

Myometrium	16.26	49.21	32.74	2.34	21.37	699.47
Omentum	16.64	25.59	21.12	3.94	12.69	267.96
Ovary	4.98	7.48	6.23	4.34	11.52	71.77
Pancreas	1.23	0	0.62	0.81	61.80	38.01
Head of Pancreas	3.57	0	1.79	1.57	31.85	56.85
Parotid Gland	0.59	0	0.30	5.48	9.12	2.69
Placenta Clontech	2.67	2.75	2.71	5.26	9.51	25.76
Prostate	9.23	7.92	8.58	3.00	16.67	142.92
Rectum	2.62	4.28	3.45	1.23	40.65	140.24
Salivary Gland Clontech	1.02	14.59	7.81	7.31	6.84	53.39
Skeletal Muscle Clontech	0	0.98	0.49	1.26	39.68	19.44
Skin	2.72	0	1.36	1.21	41.32	56.20
Small Intestine Clontech	0.99	1	1.00	0.98	51.07	50.82
Spleen	31.29	42.16	36.73	4.92	10.16	373.22
Stomach	15.74		7.87	2.73	18.32	144.14
Testis Clontech	4.63	2.77	3.70	0.57	87.87	325.13
Thymus Clontech	503.91	615.6	559.76	9.89	5.06	2829.90
Thyroid	0.75	10.38	5.57	2.77	18.05	100.45
Trachea Clontech	65.95	52.98	59.47	9.71	5.15	306.20
Urinary Bladder	9.1	3.76	6.43	5.47	9.14	58.78
Uterus	13.88	4.35	9.12	5.34	9.36	85.35

Sample sbg442445PROa	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	392.89	785.78	colon normal	
colon tumor GW98-166	21940	466.75	933.50	colon tumor	1.18799155
colon normal GW98-178	22080	113.54	227.08	colon normal	
colon tumor GW98-177	22060	43.88	87.76	colon tumor	-2.587511395
colon normal GW98-561	23514	335.16	670.32	colon normal	
colon tumor GW98-560	23513	173.85	347.70	colon tumor	-1.927868852
colon normal GW98-894	24691	288.76	577.52	colon normal	
colon tumor GW98-893	24690	164.44	328.88	colon tumor	-1.756020433
lung normal GW98-3	20742	2119.16	4238.32	lung normal	
lung tumor GW98-2	20741	33.63	67.26	lung tumor	-63.01397562
lung normal GW97-179	20677	1213.42	2426.84	lung normal	
lung tumor GW97-178	20676	2011.79	4023.58	lung tumor	1.657950256
lung normal GW98-165	21922	2088.93	4177.86	lung normal	
lung tumor GW98-164	21921	862.54	1725.08	lung tumor	-2.421835509
lung normal GW98-282	22584	499.54	999.08	lung normal	
lung tumor GW98-281	22583	946.36	1892.72	lung tumor	1.894462906
breast normal GW00-392	28750	208.96	208.96	breast normal	
breast tumor GW00-391	28746	259.34	518.68	breast tumor	2.48219755
breast normal GW00-413	28798	65.02	65.02	breast normal	

breast tumor GW00-412	28797	493.02	986.04	breast tumor	15.16517994
breast normal GW00-235:238	27592-95	24.18	24.18	breast normal	
breast tumor GW00-231:234	27588-91	126.63	126.63	breast tumor	5.236972705
breast normal GW98-621	23656	536.09	1072.18	breast normal	
breast tumor GW98-620	23655	203.7	407.40	breast tumor	-2.631762396
brain normal BB99-542	25507	88.47	176.94	brain normal	
brain normal BB99-406	25509	147.87	295.74	brain normal	
brain normal BB99-904	25546	35.13	70.26	brain normal	
brain stage 5 ALZ BB99-874	25502	75.02	150.04	brain stage 5 ALZ	-1.206211677
brain stage 5 ALZ BB99-887	25503	189	378.00	brain stage 5 ALZ	2.088628578
brain stage 5 ALZ BB99-862	25504	131.38	262.76	brain stage 5 ALZ	1.451873135
brain stage 5 ALZ BB99-927	25542	36.77	73.54	brain stage 5 ALZ	-2.46097362
CT lung KC	normal	1441.16	2882.32	CT lung	
lung 26 KC	normal	69.7	69.70	lung 26	
lung 27 KC	normal	59.95	59.95	lung 27	
lung 24 KC	COPD	5.33	5.33	lung 24	-142.0727017
lung 28 KC	COPD	30.24	30.24	lung 28	-25.04125331
lung 23 KC	COPD	52.96	52.96	lung 23	-14.29847998
lung 25 KC	COPD	17.02	17.02	lung 25	
asthmatic lung ODO3112	29321	309.94	309.94	asthmatic lung	-2.44320675
asthmatic lung ODO3433	29323	532.32	1064.64	asthmatic lung	1.405933991
asthmatic lung ODO3397	29322	1159.05	2318.10	asthmatic lung	3.061218426
asthmatic lung ODO4928	29325	873.73	1747.46	asthmatic lung	2.307647103
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		0.93	0.93	endo VEGF	0.93
endo bFGF KC		5.16	5.16	endo bFGF	5.16
heart Clontech	normal	43.01	86.02	heart	
heart (T-1) ischemic	29417	81.55	163.10	heart T-1	1.896070681
heart (T-14) non-obstructive DCM	29422	51.64	103.28	heart T-14	1.200651011
heart (T-3399) DCM	29426	90.27	180.54	heart T-3399	2.098814229
adenoid GW99-269	26162	982.05	1964.10	adenoid	
tonsil GW98-280	22582	3981.71	7963.42	tonsil	
T cells PC00314	28453	265.95	531.90	T cells	
PBMNC KC		40.89	40.89	PBMNC	
monocyte KC		62.92	125.84	monocyte	
B cells PC00665	28455	9045.58	18091.16	B cells	
dendritic cells 28441		267.47	534.94	dendritic cells	
neutrophils	28440	1212.1	1212.10	neutrophils	
eosinophils	28446	1563.76	3127.52	eosinophils	
BM unstim KC		56.55	56.55	BM unstim	

BM stim KC		27.4	27.40	BM stim	-2.063868613
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		0.92	2.30	chondrocytes	
OA Synovium IP12/01	29462	524.44	524.44	OA Synovium	
OA Synovium NP10/01	29461	191.8	383.60	OA Synovium	
OA Synovium NP57/00	28464	461.09	922.18	OA Synovium	
RA Synovium NP03/01	28466	484.63	969.26	RA Synovium	
RA Synovium NP71/00	28467	698.08	1396.16	RA Synovium	
RA Synovium NP45/00	28475	1034.78	2069.56	RA Synovium	
OA bone (biobank)	29217	547.68	547.68	OA bone (biobank)	
OA bone Sample 1	J. Emory	286.6	573.20	OA bone	
OA bone Sample 2	J. Emory	604.86	1209.72	OA bone	
Cartilage (pool)	Normal	224.68	449.36	Cartilage (pool)	
Cartilage (pool)	OA	113.78	227.56	Cartilage (pool)	-1.974687994
PBL unifected	28441	966.68	1933.36	PBL unifected	
PBL HIV IIIB	28442	1353.87	2707.74	PBL HIV IIIB	1.400535855
MRC5 uninfected (100%)	29158	1.28	2.56	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	34.07	68.14	MRC5 HSV strain F	26.6171875
W12 cells	29179	3.55	7.10	W12 cells	
Keratinocytes	29180	5.64	11.28	Keratinocytes	

Gene Name sbg442445PROa

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	1.19
colon tumor	-2.59
colon tumor	-1.93
colon tumor	-1.76
lung tumor	-63.01
lung tumor	1.66
lung tumor	-2.42
lung tumor	1.89
breast tumor	2.48
breast tumor	15.17
breast tumor	5.24
breast tumor	-2.63
brain stage 5 ALZ	-1.21
brain stage 5 ALZ	2.09
brain stage 5 ALZ	1.45
brain stage 5 ALZ	-2.46

lung 24	-142.07
lung 28	-25.04
lung 23	-14.30
asthmatic lung	-2.44
asthmatic lung	1.41
asthmatic lung	3.06
asthmatic lung	2.31
endo VEGF	0.93
endo bFGF	5.16
heart T-1	1.90
heart T-14	1.20
heart T-3399	2.10
BM stim	-2.06
osteo undif	0.00
Cartilage (pool)	-1.97
PBL HIV IIIB	1.40
MRC5 HSV strain F	26.62

Gene Name sbg456548CytoRa

Strongly expressed in adenoid/tonsils and dendritic cells. Overexpressed in stimulated bone marrow. Taken together, these data suggest a role in immune function. Expression in GI tract suggests potential role in diseases of the GI system like IBD, Chron's, etc.

Sample sbg456548CytoRa	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/ 50 ng total RNA**
Subcutaneous Adipocytes Zenbio	0.00	5.06	2.53	3.06	16.34	41.34
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	0.00	0.00	0.00	0.61	81.97	0.00
Whole Brain Clontech	0.00	0.00	0.00	7.24	6.91	0.00
Fetal Brain Clontech	0.00	0.00	0.00	0.48	103.95	0.00
Cerebellum Clontech	0.00	0.00	0.00	2.17	23.04	0.00
Cervix	0.00	7.86	3.93	2.42	20.66	81.20
Colon	9.12	37.61	23.37	2.71	18.45	431.09
Endometrium	0.00	0.00	0.00	0.73	68.21	0.00
Esophagus	0.00	0.00	0.00	1.37	36.50	0.00
Heart Clontech	0.00	0.00	0.00	1.32	37.88	0.00
Hypothalamus	0.00	0.00	0.00	0.32	155.28	0.00
Ileum	not done	39.63	39.63	2.58	19.38	768.02
Jejunum	9.16	33.67	21.42	6.60	7.58	162.23
Kidney	0.00	0.00	0.00	2.12	23.58	0.00
Liver	0.00	13.75	6.88	1.50	33.33	229.17
Fetal Liver Clontech	0.00	0.00	0.00	10.40	4.81	0.00
Lung	0.00	0.00	0.00	2.57	19.46	0.00

Mammary Gland Clontech	136.73	106.34	121.54	13.00	3.85	467.44
Myometrium	27.33	17.56	22.45	2.34	21.37	479.59
Omentum	0.00	12.61	6.31	3.94	12.69	80.01
Ovary	16.46	17.90	17.18	4.34	11.52	197.93
Pancreas	0.00	0.00	0.00	0.81	61.80	0.00
Head of Pancreas	0.00	0.00	0.00	1.57	31.85	0.00
Parotid Gland	21.25	23.72	22.49	5.48	9.12	205.16
Placenta Clontech	101.11	73.40	87.26	5.26	9.51	829.42
Prostate	8.55	0.00	4.28	3.00	16.67	71.25
Rectum	0.00	0.00	0.00	1.23	40.65	0.00
Salivary Gland Clontech	0.00	0.00	0.00	7.31	6.84	0.00
Skeletal Muscle Clontech	0.00	0.00	0.00	1.26	39.68	0.00
Skin	0.00	0.00	0.00	1.21	41.32	0.00
Small Intestine Clontech	0.00	0.00	0.00	0.98	51.07	0.00
Spleen	31.60	14.66	23.13	4.92	10.16	235.06
Stomach	0.00	7.01	3.51	2.73	18.32	64.19
Testis Clontech	0.00	0.00	0.00	0.57	87.87	0.00
Thymus Clontech	51.70	103.21	77.46	9.89	5.06	391.58
Thyroid	0.00	0.00	0.00	2.77	18.05	0.00
Trachea Clontech	0.00	0.00	0.00	9.71	5.15	0.00
Urinary Bladder	0.00	7.29	3.65	5.47	9.14	33.32
Uterus	5.98	21.02	13.50	5.34	9.36	126.40

Sample sbg456548CytoRa	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	54.19	108.38	colon normal	
colon tumor GW98-166	21940	242.87	485.74	colon tumor	4.481823215
colon normal GW98-178	22080	24.61	49.22	colon normal	
colon tumor GW98-177	22060	17.37	34.74	colon tumor	-1.416810593
colon normal GW98-561	23514	120.13	240.26	colon normal	
colon tumor GW98-560	23513	43.05	86.10	colon tumor	-2.79047619
colon normal GW98-894	24691	81.35	162.70	colon normal	
colon tumor GW98-893	24690	16.94	33.88	colon tumor	-4.802243211
lung normal GW98-3	20742	12.83	25.66	lung normal	
lung tumor GW98-2	20741	94.41	188.82	lung tumor	7.358534684
lung normal GW97-179	20677	519.7	1039.40	lung normal	
lung tumor GW97-178	20676	46.83	93.66	lung tumor	-11.09758702
lung normal GW98-165	21922	7.95	15.90	lung normal	
lung tumor GW98-164	21921	237.54	475.08	lung tumor	29.87924528
lung normal GW98-282	22584	251.04	502.08	lung normal	
lung tumor GW98-281	22583	28.16	56.32	lung tumor	-8.914772727
breast normal GW00-392	28750	138.99	138.99	breast normal	

breast tumor GW00-391	28746	147.66	295.32	breast tumor	2.124757177
breast normal GW00-413	28798	30.39	30.39	breast normal	
breast tumor GW00-412	28797	37.64	75.28	breast tumor	2.477130635
breast normal GW00-235:238	27592-95	218.09	218.09	breast normal	
breast tumor GW00-231:234	27588-91	14.68	14.68	breast tumor	-14.85626703
breast normal GW98-621	23656	1888.3	3776.60	breast normal	
breast tumor GW98-620	23655	877.2	1754.40	breast tumor	-2.152644779
brain normal BB99-542	25507	0	0.00	brain normal	
brain normal BB99-406	25509	0	0.00	brain normal	
brain normal BB99-904	25546	0	0.00	brain normal	
brain stage 5 ALZ BB99-874	25502	0	0.00	brain stage 5 ALZ	0
brain stage 5 ALZ BB99-887	25503	7.32	14.64	brain stage 5 ALZ	14.64
brain stage 5 ALZ BB99-862	25504	0	0.00	brain stage 5 ALZ	0
brain stage 5 ALZ BB99-927	25542	0	0.00	brain stage 5 ALZ	0
CT lung KC	normal	10.31	20.62	CT lung	
lung 26 KC	normal	49.79	49.79	lung 26	
lung 27 KC	normal	4.11	4.11	lung 27	
lung 24 KC	COPD	0.67	0.67	lung 24	-38.10074627
lung 28 KC	COPD	19.24	19.24	lung 28	-1.326793139
lung 23 KC	COPD	3.15	3.15	lung 23	-8.103968254
lung 25 KC	COPD	27.59	27.59	lung 25	
asthmatic lung ODO3112	29321	2.95	2.95	asthmatic lung	-8.653389831
asthmatic lung ODO3433	29323	9.86	19.72	asthmatic lung	-1.294497972
asthmatic lung ODO3397	29322	24.39	48.78	asthmatic lung	1.910880423
asthmatic lung ODO4928	29325	53.84	107.68	asthmatic lung	4.218196063
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		14.65	14.65	endo VEGF	14.65
endo bFGF KC		0	0.00	endo bFGF	0
heart Clontech	normal	0	0.00	heart	
heart (T-1) ischemic	29417	21.18	42.36	heart T-1	42.36
heart (T-14) non-obstructive DCM	29422	27.4	54.80	heart T-14	54.8
heart (T-3399) DCM	29426	93.27	186.54	heart T-3399	186.54
adenoid GW99-269	26162	579.69	1159.38	adenoid	
tonsil GW98-280	22582	3780.08	7560.16	tonsil	
T cells PC00314	28453	5.86	11.72	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		0	0.00	monocyte	
B cells PC00665	28455	19.6	39.20	B cells	
dendritic cells 28441		580.67	1161.34	dendritic	

				cells	
neutrophils	28440	19.76	19.76	neutrophils	
eosinophils	28446	15.12	30.24	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		296.72	296.72	BM stim	296.72
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		15.31	38.28	chondrocytes	
OA Synovium IP12/01	29462	39.57	39.57	OA Synovium	
OA Synovium NP10/01	29461	0	0.00	OA Synovium	
OA Synovium NP57/00	28464	70.08	140.16	OA Synovium	
RA Synovium NP03/01	28466	23.73	47.46	RA Synovium	
RA Synovium NP71/00	28467	24.13	48.26	RA Synovium	
RA Synovium NP45/00	28475	51.88	103.76	RA Synovium	
OA bone (biobank)	29217	0	0.00	OA bone (biobank)	
OA bone Sample 1	J. Emory	0	0.00	OA bone	
OA bone Sample 2	J. Emory	5.45	10.90	OA bone	
Cartilage (pool)	Normal	0	0.00	Cartilage (pool)	
Cartilage (pool)	OA	0	0.00	Cartilage (pool)	0
PBL unifected	28441	76.67	153.34	PBL unifected	
PBL HIV IIIB	28442	13.77	27.54	PBL HIV IIIB	-5.567901235
MRC5 uninfected (100%)	29158	0	0.00	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	0	0.00	MRC5 HSV strain F	0
W12 cells	29179	0	0.00	W12 cells	
Keratinocytes	29180	0	0.00	Keratinocytes	

Gene Name sbg456548CytoRa

Disease tissues	**Fold Change in Disease Population Relative to Normal**
colon tumor	4.48
colon tumor	-1.42
colon tumor	-2.79
colon tumor	-4.80
lung tumor	7.36

lung tumor	-11.10
lung tumor	29.88
lung tumor	-8.91
breast tumor	2.12
breast tumor	2.48
breast tumor	-14.86
breast tumor	-2.15
brain stage 5 ALZ	0.00
brain stage 5 ALZ	14.64
brain stage 5 ALZ	0.00
brain stage 5 ALZ	0.00
lung 24	-38.10
lung 28	-1.33
lung 23	-8.10
asthmatic lung	-8.65
asthmatic lung	-1.29
asthmatic lung	1.91
asthmatic lung	4.22
endo VEGF	14.65
endo bFGF	0.00
heart T-1	42.36
heart T-14	54.80
heart T-3399	186.54
BM stim	296.72
osteo undif	0.00
Cartilage (pool)	0.00
PBL HIV IIIB	-5.57
MRC5 HSV strain F	0.00

Gene Name sbg442358PROa

Expression in multiple immune cell types as well as stimulated bone marrow and thymus strongly suggests function in immune system. Overexpressed in breast tumors (1/4). Expression in RA and OA with corroborating expression in immune cells suggests role in these diseases. Overexpressed in heart disease suggesting role in CV diseases. Downregulated in HSV infected cells suggesting possible host cell factor.

Sample sbg442358PROa	**Mean GOI copies (sample 1)**	**Mean GOI copies (sample 2)**	**Average GOI Copies**	**18S rRNA (ng)**	**50 ng/18S rRNA (ng)**	**copies of mRNA detected/50 ng total RNA**
Subcutaneous Adipocytes Zenbio	1.86	1.71	1.79	3.06	16.34	29.17
Subcutaneous Adipose Zenbio	0.71	0.73	0.72	0.96	52.36	37.70

Adrenal Gland Clontech	3.45	1.89	2.67	0.61	81.97	218.85
Whole Brain Clontech	406.27	496.60	451.44	7.24	6.91	3117.65
Fetal Brain Clontech	3.82	1.68	2.75	0.48	103.95	285.86
Cerebellum Clontech	5.84	30.51	18.18	2.17	23.04	418.78
Cervix	2.50	0.48	1.49	2.42	20.66	30.79
Colon	18.45	18.77	18.61	2.71	18.45	343.36
Endometrium	4.93	0.30	2.62	0.73	68.21	178.38
Esophagus	8.97	6.99	7.98	1.37	36.50	291.24
Heart Clontech	5.26	16.53	10.90	1.32	37.88	412.69
Hypothalamus	2.10	2.41	2.26	0.32	155.28	350.16
Ileum	18.94	12.62	15.78	2.58	19.38	305.81
Jejunum	65.51	95.24	80.38	6.60	7.58	608.90
Kidney	2.60	3.81	3.21	2.12	23.58	75.59
Liver	7.19	7.05	7.12	1.50	33.33	237.33
Fetal Liver Clontech	1252.22	1363.06	1307.64	10.40	4.81	6286.73
Lung	27.57	6.97	17.27	2.57	19.46	335.99
Mammary Gland Clontech	79.83	72.99	76.41	13.00	3.85	293.88
Myometrium	2.46	10.62	6.54	2.34	21.37	139.74
Omentum	10.40	3.27	6.84	3.94	12.69	86.74
Ovary	17.71	31.15	24.43	4.34	11.52	281.45
Pancreas	3.33	1.74	2.54	0.81	61.80	156.67
Head of Pancreas	3.82	6.17	5.00	1.57	31.85	159.08
Parotid Gland	22.77	22.54	22.66	5.48	9.12	206.71
Placenta Clontech	14.71	53.83	34.27	5.26	9.51	325.76
Prostate	16.71	19.39	18.05	3.00	16.67	300.83
Rectum	6.71	3.49	5.10	1.23	40.65	207.32
Salivary Gland Clontech	55.38	9.30	32.34	7.31	6.84	221.20
Skeletal Muscle Clontech	3.79	4.16	3.98	1.26	39.68	157.74
Skin	4.51	14.47	9.49	1.21	41.32	392.15
Small Intestine Clontech	8.12	7.87	8.00	0.98	51.07	408.32
Spleen	14.88	17.12	16.00	4.92	10.16	162.60
Stomach	21.85	11.68	16.77	2.73	18.32	307.05
Testis Clontech	22.77	11.54	17.16	0.57	87.87	1507.47
Thymus Clontech	1990.82	1374.71	1682.77	9.89	5.06	8507.41
Thyroid	16.85	2.86	9.86	2.77	18.05	177.89
Trachea Clontech	29.69	82.85	56.27	9.71	5.15	289.75
Urinary Bladder	2.32	13.42	7.87	5.47	9.14	71.94
Uterus	8.86	11.18	10.02	5.34	9.36	93.82

Sample sbg442358PROa	**Reg number (GSK identifier)**	**Mean GOI copies**	**copies of mRNA detected/50 ng total RNA**	**Sample**	**Fold Change in Disease Population**
colon normal GW98-167	21941	1232.32	2464.64	colon normal	

colon tumor GW98-166	21940	2940.17	5880.34	colon tumor	2.385881914
colon normal GW98-178	22080	221.26	442.52	colon normal	
colon tumor GW98-177	22060	709.52	1419.04	colon tumor	3.20672512
colon normal GW98-561	23514	985.52	1971.04	colon normal	
colon tumor GW98-560	23513	829.67	1659.34	colon tumor	-1.18784577
colon normal GW98-894	24691	2738.17	5476.34	colon normal	
colon tumor GW98-893	24690	3022.06	6044.12	colon tumor	1.103678734
lung normal GW98-3	20742	536.82	1073.64	lung normal	
lung tumor GW98-2	20741	594.2	1188.40	lung tumor	1.106888715
lung normal GW97-179	20677	4382.61	8765.22	lung normal	
lung tumor GW97-178	20676	359.07	718.14	lung tumor	-12.20544741
lung normal GW98-165	21922	622.06	1244.12	lung normal	
lung tumor GW98-164	21921	1299.85	2599.70	lung tumor	2.089589429
lung normal GW98-282	22584	1782.09	3564.18	lung normal	
lung tumor GW98-281	22583	470.51	941.02	lung tumor	-3.787570934
breast normal GW00-392	28750	429	429.00	breast normal	
breast tumor GW00-391	28746	417.99	835.98	breast tumor	1.948671329
breast normal GW00-413	28798	16.03	16.03	breast normal	
breast tumor GW00-412	28797	1048.11	2096.22	breast tumor	130.768559
breast normal GW00-235:238	27592-95	2.17 -	2.17	breast normal	
breast tumor GW00-231:234	27588-91	69.91	69.91	breast tumor	32.21658986
breast normal GW98-621	23656	1037.08	2074.16	breast normal	
breast tumor GW98-620	23655	1010.59	2021.18	breast tumor	-1.026212411
brain normal BB99-542	25507	299.28	598.56	brain normal	
brain normal BB99-406	25509	250.85	501.70	brain normal	
brain normal BB99-904	25546	97.7	195.40	brain normal	
brain stage 5 ALZ BB99-874	25502	125	250.00	brain stage 5 ALZ	-1.727546667
brain stage 5 ALZ BB99-887	25503	850.01	1700.02	brain stage 5 ALZ	3.936264143
brain stage 5 ALZ BB99-862	25504	347.91	695.82	brain stage 5 ALZ	1.611117114
brain stage 5 ALZ BB99-927	25542	147.11	294.22	brain stage 5 ALZ	-1.467903836
CT lung KC	normal	130.37	260.74	CT lung	
lung 26 KC	normal	159.19	159.19	lung 26	
lung 27 KC	normal	0.49	0.49	lung 27	
lung 24 KC	COPD	2.37	2.37	lung 24	-47.89873418
lung 28 KC	COPD	45.72	45.72	lung 28	-2.482939633
lung 23 KC	COPD	20.36	20.36	lung 23	-5.575638507
lung 25 KC	COPD	33.66	33.66	lung 25	
asthmatic lung ODO3112	29321	65.46	65.46	asthmatic lung	-1.734188818
asthmatic lung ODO3433	29323	532.42	1064.84	asthmatic lung	9.380197322
asthmatic lung ODO3397	29322	2865.67	5731.34	asthmatic lung	50.48749119
asthmatic lung ODO4928	29325	494.27	988.54	asthmatic lung	8.708069063

endo cells KC	control	62.77	62.77	endo cells	
endo VEGF KC		22.41	22.41	endo VEGF	-2.800981705
endo bFGF KC		33.16	33.16	endo bFGF	-1.892943305
heart Clontech	normal	74.18	148.36	heart	
heart (T-1) ischemic	29417	270.07	540.14	heart T-1	3.640738744
heart (T-14) non-obstructive DCM	29422	680.12	1360.24	heart T-14	9.168509032
heart (T-3399) DCM	29426	414	828.00	heart T-3399	5.581019143
adenoid GW99-269	26162	781.46	1562.92	adenoid	
tonsil GW98-280	22582	2279.13	4558.26	tonsil	
T cells PC00314	28453	1129.27	2258.54	T cells	
PBMNC KC		27.98	27.98	PBMNC	
monocyte KC		3.55	7.10	monocyte	
B cells PC00665	28455	872.58	1745.16	B cells	
dendritic cells 28441		1055.22	2110.44	dendritic cells	
neutrophils	28440	740.39	740.39	neutrophils	
eosinophils	28446	1081.83	2163.66	eosinophils	
BM unstim KC		50.91	50.91	BM unstim	
BM stim KC		391.11	391.11	BM stim	7.682380672
osteo dif KC		161.31	161.31	osteo dif	
osteo undif KC		40.01	40.01	osteo undif	-4.031742064
chondrocytes		2250.59	5626.48	chondrocytes	
OA Synovium IP12/01	29462	229.19	229.19	OA Synovium	
OA Synovium NP10/01	29461	152.3	304.60	OA Synovium	
OA Synovium NP57/00	28464	413.06	826.12	OA Synovium	
RA Synovium NP03/01	28466	611.02	1222.04	RA Synovium	
RA Synovium NP71/00	28467	385.94	771.88	RA Synovium	
RA Synovium NP45/00	28475	1701.68	3403.36	RA Synovium	
OA bone (biobank)	29217	225.69	225.69	OA bone (biobank)	
OA bone Sample 1	J. Emory	306.63	613.26	OA bone	
OA bone Sample 2	J. Emory	1811.32	3622.64	OA bone	
Cartilage (pool)	Normal	384.44	768.88	Cartilage (pool)	
Cartilage (pool)	OA	174.53	349.06	Cartilage (pool)	-2.202715865
PBL unifected	28441	9016.82	18033.64	PBL unifected	
PBL HIV IIIB	28442	4331.76	8663.52	PBL HIV IIIB	-2.081560382
MRC5 uninfected (100%)	29158	2232.48	4464.96	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	419.67	839.34	MRC5 HSV strain F	-5.319608264
W12 cells	29179	3336.07	6672.14	W12 cells	
Keratinocytes	29180	5568.91	11137.82	Keratinocytes	

Gene Name sbg442358PROa

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	2.39
colon tumor	3.21
colon tumor	-1.19
colon tumor	1.10
lung tumor	1.11
lung tumor	-12.21
lung tumor	2.09
lung tumor	-3.79
breast tumor	1.95
breast tumor	130.77
breast tumor	32.22
breast tumor	-1.03
brain stage 5 ALZ	-1.73
brain stage 5 ALZ	3.94
brain stage 5 ALZ	1.61
brain stage 5 ALZ	-1.47
lung 24	-47.90
lung 28	-2.48
lung 23	-5.58
asthmatic lung	-1.73
asthmatic lung	9.38
asthmatic lung	50.49
asthmatic lung	8.71
endo VEGF	-2.80
endo bFGF	-1.89
heart T-1	3.64
heart T-14	9.17
heart T-3399	5.58
BM stim	7.68
osteo undif	-4.03
Cartilage (pool)	-2.20
PBL HIV IIIB	-2.08
MRC5 HSV strain F	-5.32

Table V. Additional diseases based on mRNA expression in specific tissues

Tissue Expression	Additional Diseases
Brain	Neurological and psychiatric diseases, including Alzheimers, parasupranuclear palsey, Huntington's disease, myotonic dystrophy, anorexia, depression, schizophrenia, headache, amnesias, anxiety disorders, sleep disorders, multiple sclerosis
Heart	Cardiovascular diseases, including congestive heart failure, dilated cardiomyopathy, cardiac arrhythmias, Hodgson's Disease, myocardial infarction, cardiac arrhythmias
Lung	Respiratory diseases, including asthma, Chronic Obstructive Pulmonary Disease, cystic fibrosis, acute bronchitis, adult respiratory distress syndrome
Liver	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, cirrhosis, hepatic encephalopathy, fatty hepatocirrhosis, viral and nonviral hepatitis, Type II Diabetes Mellitis, impaired glucose tolerance
Kidney	Renal diseases, including acute and chronic renal failure, acute tubular necrosis, cystinuria, Fanconi's Syndrome, glomerulonephritis, renal cell carcinoma, renovascular hypertension
Skeletal muscle	Eulenburg's Disease, hypoglycemia, obesity, tendinitis, periodic paralyses, malignant hyperthermia, paramyotonia congenita, myotonia congenita
Intestine	Gastrointestinal diseases, including Myotonia congenita, Ileus, Intestinal Obstruction, Tropical Sprue, Pseudomembranous Enterocolitis
Spleen/lymph	Lymphangiectasia, hypersplenism, angiomas, ankylosing spondylitis, Hodgkin's Disease, macroglobulinemia, malignant lymphomas, rheumatoid arthritis
Placenta	Choriocarcinoma, hydatidiform mole, placenta previa
Testis	Testicular cancer, male reproductive diseases, including low testosterone and male infertility
Pancreas	Diabetic ketoacidosis, Type 1 & 2 diabetes, obesity, impaired glucose tolerance

What is claimed is:

1. An isolated polypeptide selected from the group consisting of:
(a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in Table I;
(b) an isolated polypeptide comprising a polypeptide sequence set forth in Table I; and
(c) a polypeptide sequence of a gene set forth in Table I.

2. An isolated polynucleotide selected from the group consisting of:
(a) an isolated polynucleotide comprising a polynucleotide sequence set forth in Table I;
(b) an isolated polynucleotide of a gene set forth in Table I;
(c) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in Table I;
(d) an isolated polynucleotide encoding a polypeptide set forth in Table I;
(e) a polynucleotide which is an RNA equivalent of the polynucleotide of (a) to (d);
or a polynucleotide sequence complementary to said isolated polynucleotide.

3. An expression vector comprising a polynucleotide capable of producing a polypeptide of claim 1 when said expression vector is present in a compatible host cell.

4. A process for producing a recombinant host cell which comprises the step of introducing an expression vector comprising a polynucleotide capable of producing a polypeptide of claim 1 into a cell such that the host cell, under appropriate culture conditions, produces said polypeptide.

5. A recombinant host cell produced by the process of claim 4.

6. A membrane of a recombinant host cell of claim 5 expressing said polypeptide.

7. A process for producing a polypeptide which comprises culturing a host cell of claim 5 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.

SEQUENCE LISTING

<110> SMITHKLINE BEECHAM CORPORATION
SMITHKLINE BEECHAM p.l.c.
GLAXO GROUP LTD.

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<213> Homo sapiens

<400> 15
atgttgagat tctacttatt catcagtttg ttgtgcttgt caagatcaga cgcagaagaa 60
acatgtcctt cattcaccag gctgagcttt cacagtgcag tggttggtac gggactaaat 120
gtgaggctga tgctctacac aaggaaaaac ctgacctgcg cacaaaccat caactcctca 180
gcttttggga acttgaatgt gaccaagaaa accaccttca ttgtccatgg attcaggcca 240
acaggctccc ctcctgtttg gatggatgac ttagtaaagg gtttgctctc tgttgaagac 300
atgaacgtag ttgttgttga ttggaatcga ggagctacaa ctttaatata tacccatgcc 360
tctagtaaga ccagaaaagt agccatggtc ttgaaggaat ttattgacca gatgttggca 420
gaaggagctt ctcttgatga catttacatg atcggagtaa gtctaggagc ccacatatct 480
gggtttgttg gagagatgta cgatggatgg ctggggagaa ttacaggcct cgaccctgca 540
ggccctttat tcaacgggaa acctcaccaa gacagattag atcccagtga tgcgcagttt 600
gttgatgtca tccattccga cactgatgca ctgggctaca aggagccatt aggaaacata 660
gacttctacc caaatggagg attggatcaa cctggctgcc ccaaaacaat attgggagga 720
tttcagtatt ttaaatgtga ccaccagagg tctgtatacc tgtacctgtc ttccctgaga 780
gagagctgca ccatcactgc gtatccctgt gactcctacc aggattatag gaatggcaag 840
tgtgtcagct gcggcacgtc acaaaaagag tcctgtcccc ttctgggcta ttatgctgat 900
aattggaaag accatctaag ggggaaagat cctccaatga cgaaggcatt ctttgacaca 960
gctgaggaga gcccattctg catgtatcat tactttgtgg atattataac atgggacaag 1020
aatgtaagaa gaggggacat taccatcaaa ttgagagaca aagctggaaa cacccacaga 1080
tccaaaatca tcagtaatga acccaccaca tttcagaaat atcaccaagt gagtctactt 1140
gcaagattta atcaagatct ggataaagtg gctgcaattt ccttgatgtt ctctacagga 1200
tctctaatag gcccaaggta caagctcagg attctccgaa tgaagttaag gtcccttgcc 1260
catccggaga ggcctcagct gtgtcggtat gatcttgtcc tgatggaaaa cgttgaaaca 1320
gtcttccaac ctattctttg cccagagttg cagttgtaa 1359

<210> 16
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 16
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gagtgcctgg gagctgaggg ccggctggct ctcaagctgt tccgtgacct ctttgccaac 120
tacacaagtg ccctgagacc tgtggcagac acagaccaga ctctgaatgt gaccctggag 180
gtgacactgt cccagatcat cgacatggat gaacggaacc aggtgctgac cctgtatctg 240
tggatacggc aggagtggac agatgcctac ctacgatggg accccaatgc ctatggtggc 300
ctggatgcca tccgcatccc cagcagtctt gtgtggcggc cagacatcgt actctataac 360

aaagccgacg cgcagcctcc aggttccgcc agcaccaacg tggtcctgcg ccacgatggc 420
gccgtgcgct gggacgcgcc ggccatcacg cgcagctcgt gccgcgtgga tgtagcagcc 480
ttcccgttcg acgcccagca ctgcggcctg acgttcggct cctggactca cggcgggcac 540
caactggatg tgcggccgcg cggcgctgca gccagcctgg cggacttcgt ggagaacgtg 600
gagtggcgcg tgctgggcat gccggcgcgg cggcgcgtgc tcacctacgg ctgctgctcc 660
gagccctacc ccgacgtcac cttcacgctg ctgctgcgcc gccgcgccgc cgcctacgtg 720
tgcaacctgc tgctgccctg cgtgctcatc tcgctgcttg cgccgctcgc cttccacctg 780
cctgccgact caggcgagaa ggtgtcgctg ggcgtcaccg tgctgctggc gctcaccgtc 840
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tactacatgg ccactatgac catggtcaca ttctcaacag cactcaccat ccttatcatg 960
aacctgcatt actgtggtcc cagtgtccgc ccagtgccag cctgggctag ggccctcctg 1020
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aggccacctg agttatctcc tagcccccag tcgcctgaag gaggggctgg ccccccagcg 1140
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accattgcca ataccttccg cagccaccga gctgcccagc gctgccatga ggactggaag 1260
cgcctggccc gtgtgatgga ccgcttcttc ctggccatct tcttctccat ggccctggtc 1320
atgagcctcc tggtgctggt gcaggccctg tga 1353

<210> 17
<211> 768
<212> DNA
<213> Homo sapiens

<400> 17
atggttaagg gtgagaaagg ccccaagggc aagaagatca ccctcaaggt ggccaggaat 60
tgcatcaaaa tcacttttga tgggaaaaag cgccttgact tgagcaagat gggaattacc 120
accttcccca agtgtattct gcgccttagt gacatggacg agctggacct tagccggaat 180
cttatcagga agatccctga ctccatctcc aagttccaga acctccggtg gctggacctg 240
cacagcaact acatagacaa gctgcctgag tccattggcc agatgaccag cctgctctac 300
ctcaacgtca gcaacaaccg gctgaccagc aacgggctgc ccgtggagct gaagcaactc 360
aagaacatcc gcgctgtgaa cctaggcttg aaccacctgg acagcgtgcc caccacactg 420
ggggccctga aggagctcca cgaggtaggg ctccatgaca acctactgaa caacatcccc 480
gtgagcatct ccaagctccc caagctgaaa aagctcaaca taaagcggaa ccccttccca 540
aagccaggtg agtcggaaat attcatagac tccatcagga ggctggagaa cttgtatgtt 600
gtggaggaga aggatctgtg tgcggcttgc ctgagaaaat gccaaaacgc ccgggacaac 660
ctgaatagaa tcaagaacat ggccacgacg acaccgagaa agaccatctt tcccaatctg 720
atctcaccca attccatggc caaggactcc tgggaagact ggaggtga 768

<210> 18
<211> 645
<212> DNA
<213> Homo sapiens

<400> 18
atgcaggcag gaactcagtc aacgcatgag tctctgaagc ctcagagggt acaatttcag 60
tcccgaaatt ttcacaacat tttgcaatgg cagcctggga gggcacttac tggcaacagc 120
agtgtctatt ttgtgcagta caaaatatat ggacagagac aatggaaaaa taaagaagac 180
tgttggggta ctcaagaact ctcttgtgac cttaccagtg aaacctcaga catacaggaa 240
ccttattacg ggagggtgag ggcggcctcg gctgggagct actcagaatg gagcatgacg 300
ccgcggttca ctccctggtg ggaaacaaaa atagatcctc cagtcatgaa tataacccaa 360
gtcaatggct ctttgttggt aattctccat gctccaaatt taccatatag ataccaaaag 420
gaaaaaaatg tatctataga agattactat gaactactat accgagtttt tataattaac 480
aattcactag aaaaggagca aaaggtttat gaaggggctc acagagcggt tgaaattgaa 540
gctctaacac cacactccag ctactgtgta gtggctgaaa tatatcagcc catgttagac 600
agaagaagtc agagaagtga agagagatgt gtggaaattc catga 645

<210> 19
<211> 696
<212> DNA

<213> Homo sapiens

<400> 19
atgatgccta aacattgctt tctaggcttc ctcatcagtt tcttccttac tggtgtagca 60
ggaactcagt caacgcatga gtctctgaag cctcagaggg tacaatttca gtcccgaaat 120
tttcacaaca ttttgcaatg gcagcctggg agggcactta ctggcaacag cagtgtctat 180
tttgtgcagt acaaaatata tggacagaga caatggaaaa ataaagaaga ctgttggggt 240
actcaagaac tctcttgtga ccttaccagt gaaacctcag acatacagga accttattac 300
gggagggtga gggcggcctc ggctgggagc tactcagaat ggagcatgac gccgcggttc 360
actccctggt gggaaacaaa aatagatcct ccagtcatga atataaccca agtcaatggc 420
tctttgttgg taattctcca tgctccaaat ttaccatata gataccaaaa ggaaaaaaat 480
gtatctatag aagattacta tgaactacta taccgagttt ttataattaa caattcacta 540
gaaaaggagc aaaaggttta tgaaggggct cacagagcgg ttgaaattga agctctaaca 600
ccacactcca gctactgtgt agtggctgaa atatatcagc ccatgttaga cagaagaagt 660
cagagaagtg aagagagatg tgtggaaatt ccatga 696

<210> 20
<211> 792
<212> DNA
<213> Homo sapiens

<400> 20
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ggaactcagt caacgcatga gtctctgaag cctcagaggg tacaatttca gtcccgaaat 120
tttcacaaca ttttgcaatg gcagcctggg agggcactta ctggcaacag cagtgtctat 180
tttgtgcagt acaaaatcat gttctcatgc agcatgaaaa gctctcacca gaagccaagt 240
ggatgctggc agcacatttc ttgtaacttc ccaggctgca gaacattggc taaatatgga 300
cagagacaat ggaaaaataa agaagactgt tggggtactc aagaactctc ttgtgacctt 360
accagtgaaa cctcagacat acaggaacct tattacggga gggtgagggc ggcctcggct 420
gggagctact cagaatggag catgacgccg cggttcactc cctggtggga aacaaaaata 480
gatcctccag tcatgaatat aacccaagtc aatggctctt tgttggtaat tctccatgct 540
ccaaatttac catatagata ccaaaaggaa aaaaatgtat ctatagaaga ttactatgaa 600
ctactatacc gagtttttat aattaacaat tcactagaaa aggagcaaaa ggtttatgaa 660
ggggctcaca gagcggttga aattgaagct ctaacaccac actccagcta ctgtgtagtg 720
gctgaaatat atcagcccat gttagacaga agaagtcaga gaagtgaaga gagatgtgtg 780
gaaattccat ga 792

<210> 21
<211> 780
<212> DNA
<213> Homo sapiens

<400> 21
atgtatgtat tatctccagt ggaatttata attctacaac ttttatttat tcaggccatt 60
tccagcagtt taaaaggttt cctttcagct atgagactgg ctcatagagg ctgtaatgtt 120
gatacaccag tttcaacgct cacaccagtg aagacttcag aatttgaaaa ctttaaaact 180
aaaatggtta tcacatccaa aaaagactat cctctaagta agaattttcc atattccttg 240
gaacatcttc agacttctta ctgtgggctt gtccgagttg atatgcgtat gctttgctta 300
aaaagcctta ggaaattaga cttgagtcac aaccatataa aaaagcttcc agctacaatt 360
ggagacctca tacaccttca agaacttaac ctgaatgaca atcacttgga gtcatttagt 420
gtagccttgt gtcattctac actccagaag tcacttcgga gtttggacct cagcaagaac 480
aaaatcaagg cactccctgt gcagttttgc cagctccagg aacttaagaa tttaaaactt 540
gacgataatg aattgattca atttccttgc aagataggac aactaataaa ccttcgcttt 600
ttgtcagcag ctcgaaataa gcttccattt ttgcctagtg aatttagaaa tttatccctt 660
gaatacttgg atctttttgg aaatactttt gaacaaccaa aagtccttcc agtaataaag 720
ctgcaagcac cattaacttt attggaatct tctgcacgaa ccatattaca taataggtaa 780

<210> 22

<211> 1251
<212> DNA
<213> Homo sapiens

<400> 22
atgaagctac actgtgaggt ggaggtgatc agccggcact tgcccgcctt ggggcttagg 60
aaccggggca agggcgtccg agccgtgttg agcctctgtc agcagacttc caggagtcag 120
ccgccggtcc gagccttcct gctcatctcc accctgaagg acaagcgcgg gacccgctat 180
gagctaaggg agaacattga gcaattcttc accaaatttg tagatgaggg gaaagccact 240
gttcggttaa aggagcctcc tgtggatatc tgtctaagta aggccatttc cagcagttta 300
aaaggtttcc tttcagctat gagactggct catagaggct gtaatgttga tacaccagtt 360
tcaacgctca caccagtgaa gacttcagaa tttgaaaact ttaaaactaa aatggttatc 420
acatccaaaa aagactatcc tctaagtaag aattttccat attccttgga acatcttcag 480
acttcttact gtgggcttgt ccgagttgat atgcgtatgc tttgcttaaa aagccttagg 540
aaattagact tgagtcacaa ccatataaaa aagcttccag ctacaattgg agacctcata 600
caccttcaag aacttaacct gaatgacaat cacttggagt catttagtgt agccttgtgt 660
cattctacac tccagaagtc acttcggagt ttggacctca gcaagaacaa aatcaaggca 720
ctccctgtgc agttttgcca gctccaggaa cttaagaatt taaaacttga cgataatgaa 780
ttgattcaat ttccttgcaa gataggacaa ctaataaacc ttcgcttttt gtcagcagct 840
cgaaataagc ttccattttt gcctagtgaa tttagaaatt tatcccttga atacttggat 900
ctttttggaa atacttttga acaaccaaaa gtccttccag taataaagct gcaagcacca 960
ttaactttat tggaatcttc tgcacgaacc atattacata ataggaatag gattccatat 1020
ggctctcata tcattccatt ccatctctgc caagatttgg ataccgcaaa aatttgtgtt 1080
tgtggaagat tctgtctgaa ctctttcatt caaggaacta ctaccatgaa tctgcattct 1140
gttgcccaca ctgtggtctt agtagataat ttgggtggta ctgaagcacc tattatctct 1200
tatttctgtt ctctaggctg ttatgttaat tcctctgata tgttaaagta a 1251

<210> 23
<211> 461
<212> PRT
<213> Homo sapiens

<400> 23
Met Leu Gly Ile Trp Ile Val Ala Phe Leu Phe Phe Gly Thr Ser Arg
1 5 10 15
Gly Lys Glu Val Cys Tyr Glu Arg Leu Gly Cys Phe Lys Asp Gly Leu
20 25 30
Pro Trp Thr Arg Thr Phe Ser Thr Glu Leu Val Gly Leu Pro Trp Ser
35 40 45
Pro Glu Lys Ile Asn Thr Arg Phe Leu Leu Tyr Thr Ile His Asn Pro
50 55 60
Asn Ala Tyr Gln Glu Ile Ser Ala Val Asn Ser Ser Thr Ile Gln Ala
65 70 75 80
Ser Tyr Phe Gly Thr Asp Lys Ile Thr Arg Ile Asn Ile Ala Gly Trp
85 90 95
Lys Thr Asp Gly Lys Trp Gln Arg Asp Met Cys Asn Val Leu Leu Gln
100 105 110
Leu Glu Asp Ile Asn Cys Ile Asn Leu Asp Trp Ile Asn Gly Ser Arg
115 120 125
Glu Tyr Ile His Ala Val Asn Asn Leu Arg Val Val Gly Ala Glu Val
130 135 140
Ala Tyr Phe Ile Asp Val Leu Met Lys Lys Phe Glu Tyr Ser Pro Ser
145 150 155 160
Lys Val His Leu Ile Gly His Ser Leu Gly Ala His Leu Ala Gly Glu
165 170 175
Ala Gly Ser Arg Ile Pro Gly Leu Gly Arg Ile Thr Gly Leu Asp Pro
180 185 190
Ala Gly Pro Phe Phe His Asn Thr Pro Lys Glu Val Arg Leu Asp Pro
195 200 205

```
Ser Asp Ala Asn Phe Val Asp Val Ile His Thr Asn Ala Ala Arg Ile
    210                 215                 220
Leu Phe Glu Leu Gly Val Gly Thr Ile Asp Ala Cys Gly His Leu Asp
225                 230                 235                 240
Phe Tyr Pro Asn Gly Gly Lys His Met Pro Gly Cys Glu Asp Leu Ile
                245                 250                 255
Thr Pro Leu Leu Lys Phe Asn Phe Asn Ala Tyr Lys Lys Glu Met Ala
            260                 265                 270
Ser Phe Phe Asp Cys Asn His Ala Arg Ser Tyr Gln Phe Tyr Ala Glu
        275                 280                 285
Ser Ile Leu Asn Pro Asp Ala Phe Ile Ala Tyr Pro Cys Arg Ser Tyr
    290                 295                 300
Thr Ser Phe Lys Ala Gly Thr Cys Val Gly Cys Ala Asp Leu Leu His
305                 310                 315                 320
Arg Ile Asp Lys Ile Gly Ser His Thr Ser His Val Phe Leu Thr Leu
                325                 330                 335
Ser Leu Pro Phe Leu Leu Val Ser Leu Tyr Leu Gly Trp Arg His Lys
            340                 345                 350
Leu Ser Val Lys Leu Ser Gly Ser Glu Val Thr Gln Gly Thr Val Phe
        355                 360                 365
Leu Arg Val Gly Gly Ala Val Arg Lys Thr Gly Glu Phe Ala Ile Val
    370                 375                 380
Ser Gly Lys Leu Glu Pro Gly Met Thr Tyr Thr Lys Leu Ile Asp Ala
385                 390                 395                 400
Asp Val Asn Val Gly Asn Ile Thr Ser Val Gln Phe Ile Trp Lys Lys
                405                 410                 415
His Leu Phe Glu Asp Ser Gln Asn Lys Leu Gly Ala Glu Met Val Ile
            420                 425                 430
Asn Thr Ser Gly Lys Tyr Gly Tyr Lys Ser Thr Phe Cys Ser Gln Asp
        435                 440                 445
Ile Met Gly Pro Asn Ile Leu Gln Asn Leu Lys Pro Cys
    450                 455                 460
```

<210> 24
<211> 308
<212> PRT
<213> Homo sapiens

<400> 24

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Met Pro Phe Leu Gln Leu Lys Gly Arg Ala Thr Pro Pro Ser Trp Arg
 1                  5                  10                  15
His Asp Ser Arg Ser Leu Val His Leu Leu Asp Gly Lys Glu Gly Val
            20                  25                  30
Trp Asp Thr Thr Gly Tyr Ala Leu Gly Ser Arg Glu Ser Leu Asn Pro
        35                  40                  45
Asp Met Gly Ile Gly Asp Pro His Gly His Ser Thr Val His Thr Arg
    50                  55                  60
Glu Ala Gly Thr Ala Cys Pro Leu Gln Leu Leu Gly Ala Arg Glu Ala
65                  70                  75                  80
Ser Leu Leu Ala Cys Gly Ile Cys Gln Ala Ser Gly Gln Ile Phe Ile
                85                  90                  95
Thr Gln Thr Leu Gly Ile Lys Gly Tyr Arg Thr Val Val Ala Leu Asp
            100                 105                 110
Lys Val Pro Glu Asp Val Gln Glu Tyr Ser Trp Tyr Trp Gly Ala Asn
        115                 120                 125
Asp Ser Ala Gly Asn Met Ile Ile Ser His Lys Pro Pro Ser Ala Gln
    130                 135                 140
Gln Pro Gly Pro Met Tyr Thr Gly Arg Glu Arg Val Asn Arg Glu Gly
```

```
145                 150                 155                 160
Ser Leu Leu Ile Arg Pro Thr Ala Leu Asn Asp Thr Gly Asn Tyr Thr
                165                 170                 175
Val Arg Val Val Ala Gly Asn Glu Thr Gln Arg Ala Thr Gly Trp Leu
            180                 185                 190
Glu Val Leu Asp Gly Pro Asp Tyr Val Leu Leu Arg Ser Asn Pro Asp
        195                 200                 205
Asp Phe Asn Gly Ile Val Thr Ala Glu Ile Gly Ser Gln Val Glu Met
    210                 215                 220
Glu Cys Ile Cys Tyr Ser Phe Leu Asp Leu Lys Tyr His Trp Ile His
225                 230                 235                 240
Asn Gly Ser Leu Leu Asn Phe Ser Asp Ala Lys Met Asn Leu Ser Ser
                245                 250                 255
Leu Ala Trp Glu Gln Met Gly Arg Tyr Arg Cys Thr Val Glu Asn Pro
            260                 265                 270
Val Thr Gln Leu Ile Met Tyr Met Asp Val Arg Ile Gln Ala Pro His
        275                 280                 285
Glu Cys Ser Ser Ser Pro Pro Gly Ser Cys Phe Ala His Leu Pro Ala
    290                 295                 300
Ser Met Pro Cys
305
```

<210> 25
<211> 457
<212> PRT
<213> Homo sapiens

<400> 25

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Met Asp Leu Ser Arg Pro Arg Trp Ser Leu Trp Arg Arg Val Phe Leu
 1               5                  10                  15
Met Ala Ser Leu Leu Ala Cys Gly Ile Cys Gln Ala Ser Gly Gln Ile
            20                  25                  30
Phe Ile Thr Gln Thr Leu Gly Ile Lys Gly Tyr Arg Thr Val Val Ala
        35                  40                  45
Leu Asp Lys Val Pro Glu Asp Val Gln Glu Tyr Ser Trp Tyr Trp Gly
    50                  55                  60
Ala Asn Asp Ser Ala Gly Asn Met Ile Ile Ser His Lys Pro Pro Ser
65                  70                  75                  80
Ala Gln Gln Pro Gly Pro Met Tyr Thr Gly Arg Glu Arg Val Asn Arg
                85                  90                  95
Glu Gly Ser Leu Leu Ile Arg Pro Thr Ala Leu Asn Asp Thr Gly Asn
            100                 105                 110
Tyr Thr Val Arg Val Val Ala Gly Asn Glu Thr Gln Arg Ala Thr Gly
        115                 120                 125
Trp Leu Glu Val Leu Glu Leu Gly Ser Asn Leu Gly Ile Ser Val Asn
    130                 135                 140
Ala Ser Ser Leu Val Glu Asn Met Asp Ser Val Ala Ala Asp Cys Leu
145                 150                 155                 160
Thr Asn Val Thr Asn Ile Thr Trp Tyr Val Asn Asp Val Pro Thr Ser
                165                 170                 175
Ser Ser Asp Arg Met Thr Ile Ser Pro Asp Gly Lys Thr Leu Val Ile
            180                 185                 190
Leu Arg Val Ser Arg Tyr Asp Arg Thr Ile Gln Cys Met Ile Glu Ser
        195                 200                 205
Phe Pro Glu Ile Phe Gln Arg Ser Glu Arg Ile Ser Leu Thr Val Ala
    210                 215                 220
Tyr Gly Pro Asp Tyr Val Leu Leu Arg Ser Asn Pro Asp Asp Phe Asn
225                 230                 235                 240
```

```
Gly Ile Val Thr Ala Glu Ile Gly Ser Gln Val Glu Met Glu Cys Ile
                245                 250                 255
Cys Tyr Ser Phe Leu Asp Leu Lys Tyr His Trp Ile His Asn Gly Ser
            260                 265                 270
Leu Leu Asn Phe Ser Asp Ala Lys Met Asn Leu Ser Ser Leu Ala Trp
        275                 280                 285
Glu Gln Met Gly Arg Tyr Arg Cys Thr Val Glu Asn Pro Val Thr Gln
    290                 295                 300
Leu Ile Met Tyr Met Asp Val Arg Ile Gln Ala Pro His Glu Cys Pro
305                 310                 315                 320
Leu Pro Ser Gly Ile Leu Pro Val Val His Arg Asp Phe Ser Ile Ser
                325                 330                 335
Gly Ser Met Val Met Phe Leu Ile Met Leu Thr Val Leu Gly Gly Val
            340                 345                 350
Tyr Ile Cys Gly Val Leu Ile His Ala Leu Ile Asn His Tyr Ser Ile
        355                 360                 365
Arg Cys Pro His Cys Ser Gly Thr Arg Val Gly Cys Trp Leu Gly Ala
    370                 375                 380
Gly Thr Gln Glu Pro Ala Leu Pro Pro Glu Gly Lys Gln Ser Gln Lys
385                 390                 395                 400
Gly Arg Asp Lys Pro Gly Thr Arg Leu Ser Gly Ile Ile Trp Gly Arg
                405                 410                 415
Gln Ile Ser Pro Gln Asp Leu Lys Leu Met Gly Ala Arg Glu Gly Leu
            420                 425                 430
Glu Ser Ala Met Val Leu Asn Ser Cys Gly Val Ser Ser Ser Asn Phe
        435                 440                 445
Pro Ser Leu Cys Val Tyr Lys Gly Tyr
    450                 455
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<210> 26
<211> 704
<212> PRT
<213> Homo sapiens

<400> 26

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Met Leu His Asp Gly Leu Thr Ala Pro Asp Gly Cys Gly Ile Tyr Ser
 1               5                  10                  15
Leu Thr Gly Arg Glu Val Leu Thr Pro Phe Pro Gly Leu Gly Thr Ala
            20                  25                  30
Ala Ala Pro Ala Gln Gly Gly Ala His Leu Lys Gln Cys Asp Leu Leu
        35                  40                  45
Lys Leu Ser Arg Arg Gln Lys Gln Leu Cys Arg Arg Glu Pro Gly Leu
    50                  55                  60
Ala Glu Thr Leu Arg Asp Ala Ala His Leu Gly Leu Leu Glu Cys Gln
65                  70                  75                  80
Phe Gln Phe Arg His Glu Arg Trp Asn Cys Ser Leu Glu Gly Arg Met
                85                  90                  95
Gly Leu Leu Lys Arg Gly Phe Lys Glu Thr Ala Phe Leu Tyr Ala Val
            100                 105                 110
Ser Ser Ala Ala Leu Thr His Thr Leu Ala Arg Ala Cys Ser Ala Gly
        115                 120                 125
Arg Met Glu Arg Cys Thr Cys Asp Asp Ser Pro Gly Leu Glu Ser Arg
    130                 135                 140
Gln Ala Trp Gln Trp Gly Val Cys Gly Asp Asn Leu Lys Tyr Ser Thr
145                 150                 155                 160
Lys Phe Leu Ser Asn Phe Leu Gly Ser Lys Arg Gly Asn Lys Asp Leu
                165                 170                 175
Arg Ala Arg Ala Asp Ala His Asn Thr His Val Gly Ile Lys Ala Val
```

180 185 190
Lys Ser Gly Leu Arg Thr Thr Cys Lys Cys His Gly Val Ser Gly Ser
195 200 205
Cys Ala Val Arg Thr Cys Trp Lys Gln Leu Ser Pro Phe Arg Glu Thr
210 215 220
Gly Gln Val Leu Lys Leu Arg Tyr Asp Ser Ala Val Lys Val Ser Ser
225 230 235 240
Ala Thr Asn Glu Ala Leu Gly Arg Leu Glu Leu Trp Ala Pro Ala Arg
245 250 255
Gln Gly Ser Leu Thr Lys Gly Leu Ala Pro Arg Ser Gly Asp Leu Val
260 265 270
Tyr Met Glu Asp Ser Pro Ser Phe Cys Arg Pro Ser Lys Tyr Ser Pro
275 280 285
Gly Thr Ala Gly Arg Val Cys Ser Arg Glu Ala Ser Cys Ser Ser Leu
290 295 300
Cys Cys Gly Arg Gly Tyr Asp Thr Gln Ser Arg Leu Val Ala Phe Ser
305 310 315 320
Cys His Cys Gln Val Gln Trp Cys Cys Tyr Val Glu Cys Gln Gln Cys
325 330 335
Val Gln Glu Glu Leu Val Tyr Thr Cys Lys His Ala Met Gly Pro Val
340 345 350
Gly Phe Pro Arg Gln Cys Gln Gly Ala Phe Phe Glu Ser Ser Pro Gly
355 360 365
Gln Thr Arg Ala Arg Leu Thr Gly Arg Glu Val Leu Thr Pro Phe Pro
370 375 380
Gly Leu Gly Thr Ala Ala Ala Pro Ala Gln Gly Gly Ala His Leu Lys
385 390 395 400
Gln Cys Asp Leu Leu Lys Leu Ser Arg Arg Gln Lys Gln Leu Cys Arg
405 410 415
Arg Glu Pro Gly Leu Ala Glu Thr Leu Arg Asp Ala Ala His Leu Gly
420 425 430
Leu Leu Glu Cys Gln Phe Gln Phe Arg His Glu Arg Trp Asn Cys Ser
435 440 445
Leu Glu Gly Arg Met Gly Leu Leu Lys Arg Gly Phe Lys Glu Thr Ala
450 455 460
Phe Leu Tyr Ala Val Ser Ser Ala Ala Leu Thr His Thr Leu Ala Arg
465 470 475 480
Ala Cys Ser Ala Gly Arg Met Glu Arg Cys Thr Cys Asp Asp Ser Pro
485 490 495
Gly Leu Glu Ser Arg Gln Ala Trp Gln Trp Gly Val Cys Gly Asp Asn
500 505 510
Leu Lys Tyr Ser Thr Lys Phe Leu Ser Asn Phe Leu Gly Ser Lys Arg
515 520 525
Gly Asn Lys Asp Leu Arg Ala Arg Ala Asp Ala His Asn Thr His Val
530 535 540
Gly Ile Lys Ala Val Lys Ser Gly Leu Arg Thr Thr Cys Lys Cys His
545 550 555 560
Gly Val Ser Gly Ser Cys Ala Val Arg Thr Cys Trp Lys Gln Leu Ser
565 570 575
Pro Phe Arg Glu Thr Gly Gln Val Leu Lys Leu Arg Tyr Asp Ser Ala
580 585 590
Val Lys Val Ser Ser Ala Thr Asn Glu Ala Leu Gly Arg Leu Glu Leu
595 600 605
Trp Ala Pro Ala Arg Gln Gly Ser Leu Thr Lys Gly Leu Ala Pro Arg
610 615 620
Ser Gly Asp Leu Val Tyr Met Glu Asp Ser Pro Ser Phe Cys Arg Pro
625 630 635 640
Ser Lys Tyr Ser Pro Gly Thr Ala Gly Arg Val Cys Ser Arg Glu Ala
645 650 655

```
Ser Cys Ser Ser Leu Cys Cys Gly Arg Gly Tyr Asp Thr Gln Ser Arg
            660                 665                 670
Leu Val Ala Phe Ser Cys His Cys Gln Val Gln Trp Cys Cys Tyr Val
        675                 680                 685
Glu Cys Gln Gln Cys Val Gln Glu Glu Leu Val Tyr Thr Cys Lys His
    690                 695                 700
```

<210> 27
<211> 361
<212> PRT
<213> Homo sapiens

<400> 27

```
Met Lys Pro Leu Arg Arg Pro Leu Pro Phe Ile Cys Pro Ser Pro Pro
 1               5                  10                  15
Ser Pro Arg Leu Thr Cys Leu Pro Pro Leu Ala Leu Ser Ser Leu Thr
            20                  25                  30
Gly Arg Glu Val Leu Thr Pro Phe Pro Gly Leu Gly Thr Ala Ala Ala
        35                  40                  45
Pro Ala Gln Gly Gly Ala His Leu Lys Gln Cys Asp Leu Leu Lys Leu
    50                  55                  60
Ser Arg Arg Gln Lys Gln Leu Cys Arg Arg Glu Pro Gly Leu Ala Glu
65                  70                  75                  80
Thr Leu Arg Asp Ala Ala His Leu Gly Leu Leu Glu Cys Gln Phe Gln
                85                  90                  95
Phe Arg His Glu Arg Trp Asn Cys Ser Leu Glu Gly Arg Met Gly Leu
            100                 105                 110
Leu Lys Arg Gly Phe Lys Glu Thr Ala Phe Leu Tyr Ala Val Ser Ser
        115                 120                 125
Ala Ala Leu Thr His Thr Leu Ala Arg Ala Cys Ser Ala Gly Arg Met
    130                 135                 140
Glu Arg Cys Thr Cys Asp Asp Ser Pro Gly Leu Glu Ser Arg Gln Ala
145                 150                 155                 160
Trp Gln Trp Gly Val Cys Gly Asp Asn Leu Lys Tyr Ser Thr Lys Phe
                165                 170                 175
Leu Ser Asn Phe Leu Gly Ser Lys Arg Gly Asn Lys Asp Leu Arg Ala
            180                 185                 190
Arg Ala Asp Ala His Asn Thr His Val Gly Ile Lys Ala Val Lys Ser
        195                 200                 205
Gly Leu Arg Thr Thr Cys Lys Cys His Gly Val Ser Gly Ser Cys Ala
    210                 215                 220
Val Arg Thr Cys Trp Lys Gln Leu Ser Pro Phe Arg Glu Thr Gly Gln
225                 230                 235                 240
Val Leu Lys Leu Arg Tyr Asp Ser Ala Val Lys Val Ser Ser Ala Thr
                245                 250                 255
Asn Glu Ala Leu Gly Arg Leu Glu Leu Trp Ala Pro Ala Arg Gln Gly
            260                 265                 270
Ser Leu Thr Lys Gly Leu Ala Pro Arg Ser Gly Asp Leu Val Tyr Met
        275                 280                 285
Glu Asp Ser Pro Ser Phe Cys Arg Pro Ser Lys Tyr Ser Pro Gly Thr
    290                 295                 300
Ala Gly Arg Val Cys Ser Arg Glu Ala Ser Cys Ser Ser Leu Cys Cys
305                 310                 315                 320
Gly Arg Gly Tyr Asp Thr Gln Ser Arg Leu Val Ala Phe Ser Cys His
                325                 330                 335
Cys Gln Val Gln Trp Cys Cys Tyr Val Glu Cys Gln Gln Cys Val Gln
            340                 345                 350
Glu Glu Leu Val Tyr Thr Cys Lys His
```

355 360

<210> 28
<211> 365
<212> PRT
<213> Homo sapiens

<400> 28
Met Trp Leu Leu Leu Thr Thr Thr Cys Leu Ile Cys Gly Thr Leu Asn
1 5 10 15
Ala Gly Gly Phe Leu Asp Leu Glu Asn Glu Val Asn Pro Glu Val Trp
20 25 30
Met Asn Thr Ser Glu Ile Ile Ile Tyr Asn Gly Tyr Pro Ser Glu Glu
35 40 45
Tyr Glu Val Thr Thr Glu Asp Gly Tyr Ile Leu Leu Val Asn Arg Ile
50 55 60
Pro Tyr Gly Arg Thr His Ala Arg Ser Thr Ala Asp Ala Gly Tyr Asp
65 70 75 80
Val Trp Met Gly Asn Ser Arg Gly Asn Thr Trp Ser Arg Arg His Lys
85 90 95
Thr Leu Ser Glu Thr Asp Glu Lys Phe Trp Ala Phe Ser Phe Asp Glu
100 105 110
Met Ala Lys Tyr Asp Leu Pro Gly Val Ile Asp Phe Ile Val Asn Lys
115 120 125
Thr Gly Gln Glu Lys Leu Tyr Phe Ile Gly His Ser Leu Gly Thr Thr
130 135 140
Ile Gly Phe Val Ala Phe Ser Thr Met Pro Glu Leu Ala Gln Arg Ile
145 150 155 160
Lys Met Asn Phe Ala Leu Gly Pro Thr Ile Ser Phe Lys Tyr Pro Thr
165 170 175
Gly Ile Phe Thr Arg Phe Phe Leu Leu Pro Asn Ser Ile Ile Lys Ala
180 185 190
Val Phe Gly Thr Lys Gly Phe Phe Leu Glu Asp Lys Lys Thr Lys Ile
195 200 205
Ala Ser Thr Lys Ile Cys Asn Asn Lys Ile Leu Trp Leu Ile Cys Ser
210 215 220
Glu Phe Met Ser Leu Trp Ala Gly Ser Asn Lys Lys Asn Met Asn Gln
225 230 235 240
Ser Arg Met Asp Val Tyr Met Ser His Ala Pro Thr Gly Ser Ser Val
245 250 255
His Asn Ile Leu His Ile Lys Gln Leu Tyr His Ser Asp Glu Phe Arg
260 265 270
Ala Tyr Asp Trp Gly Asn Asp Ala Asp Asn Met Lys His Tyr Asn Gln
275 280 285
Ser His Pro Pro Ile Tyr Asp Leu Thr Ala Met Lys Val Pro Thr Ala
290 295 300
Ile Trp Ala Gly Gly His Asp Val Leu Val Thr Pro Gln Asp Val Ala
305 310 315 320
Arg Ile Leu Pro Gln Ile Lys Ser Leu His Tyr Phe Lys Leu Leu Pro
325 330 335
Asp Trp Asn His Phe Asp Phe Val Trp Gly Leu Asp Ala Pro Gln Arg
340 345 350
Met Tyr Ser Glu Ile Ile Ala Leu Met Lys Ala Tyr Ser
355 360 365

<210> 29
<211> 397

<212> PRT
<213> Homo sapiens

<400> 29

```
Met Trp Gln Leu Leu Ala Ala Ala Cys Trp Met Leu Leu Leu Gly Ser
 1               5                  10                  15
Met Tyr Gly Tyr Asp Lys Lys Gly Asn Asn Ala Asn Pro Glu Ala Asn
            20                  25                  30
Met Asn Ile Ser Gln Ile Ile Ser Tyr Trp Gly Tyr Pro Tyr Glu Glu
        35                  40                  45
Tyr Asp Val Thr Thr Lys Asp Gly Tyr Ile Leu Gly Ile Tyr Arg Ile
    50                  55                  60
Pro His Gly Arg Gly Cys Pro Gly Arg Thr Ala Pro Lys Pro Ala Val
65                  70                  75                  80
Tyr Leu Gln His Gly Leu Ile Ala Ser Ala Ser Asn Trp Ile Cys Asn
                85                  90                  95
Leu Pro Asn Asn Ser Leu Ala Phe Leu Leu Ala Asp Ser Gly Tyr Asp
            100                 105                 110
Val Trp Leu Gly Asn Ser Arg Gly Asn Thr Trp Ser Arg Lys His Leu
        115                 120                 125
Lys Leu Ser Pro Lys Ser Pro Glu Tyr Trp Ala Phe Ser Leu Asp Glu
    130                 135                 140
Met Ala Lys Tyr Asp Leu Pro Ala Thr Ile Asn Phe Ile Ile Glu Lys
145                 150                 155                 160
Thr Gly Gln Lys Arg Leu Tyr Tyr Val Gly His Ser Gln Gly Thr Thr
                165                 170                 175
Ile Ala Phe Ile Ala Phe Ser Thr Asn Pro Glu Leu Ala Lys Lys Ile
            180                 185                 190
Lys Ile Phe Phe Ala Leu Ala Pro Val Val Thr Val Lys Tyr Thr Gln
        195                 200                 205
Ser Pro Met Lys Lys Leu Thr Thr Leu Ser Arg Arg Val Val Lys Val
    210                 215                 220
Leu Phe Gly Asp Lys Met Phe His Pro His Thr Leu Phe Asp Gln Phe
225                 230                 235                 240
Ile Ala Thr Lys Val Cys Asn Arg Lys Leu Phe Arg Arg Ile Cys Ser
                245                 250                 255
Asn Phe Leu Phe Thr Leu Ser Gly Phe Asp Pro Gln Asn Leu Asn Met
            260                 265                 270
Ser Arg Leu Asp Val Tyr Leu Ser His Asn Pro Ala Gly Thr Ser Val
        275                 280                 285
Gln Asn Met Leu His Trp Ala Gln Leu Tyr His Ser Asp Glu Phe Arg
    290                 295                 300
Ala Tyr Asp Trp Gly Asn Asp Ala Asp Asn Met Lys His Tyr Asn Gln
305                 310                 315                 320
Ser His Pro Pro Ile Tyr Asp Leu Thr Ala Met Lys Val Pro Thr Ala
                325                 330                 335
Ile Trp Ala Gly Gly His Asp Val Leu Val Thr Pro Gln Asp Val Ala
            340                 345                 350
Arg Ile Leu Pro Gln Ile Lys Ser Leu His Tyr Phe Lys Leu Leu Pro
        355                 360                 365
Asp Trp Asn His Phe Asp Phe Val Trp Gly Leu Asp Ala Pro Gln Arg
    370                 375                 380
Met Tyr Ser Glu Ile Ile Ala Leu Met Lys Ala Tyr Ser
385                 390                 395
```

<210> 30
<211> 3705
<212> PRT

<213> Homo sapiens

<400> 30

```
Met Ala Lys Arg Leu Cys Ala Gly Ser Ala Leu Cys Val Arg Gly Pro
 1               5                  10                  15
Arg Gly Pro Ala Pro Leu Leu Leu Val Gly Leu Ala Leu Leu Gly Ala
            20                  25                  30
Ala Arg Ala Arg Glu Glu Ala Gly Gly Gly Phe Ser Leu His Pro Pro
        35                  40                  45
Tyr Phe Asn Leu Ala Glu Gly Ala Arg Ile Ala Ala Ser Ala Thr Cys
    50                  55                  60
Gly Glu Glu Ala Pro Ala Arg Gly Ser Pro Arg Pro Thr Glu Asp Leu
65                  70                  75                  80
Tyr Cys Lys Leu Val Gly Gly Pro Val Ala Gly Gly Asp Pro Asn Gln
                85                  90                  95
Thr Ile Arg Gly Gln Tyr Cys Asp Ile Cys Thr Ala Ala Asn Ser Asn
            100                 105                 110
Lys Ala His Pro Ala Ser Asn Ala Ile Asp Gly Thr Glu Arg Trp Trp
        115                 120                 125
Gln Ser Pro Pro Leu Ser Arg Gly Leu Glu Tyr Asn Glu Val Asn Val
    130                 135                 140
Thr Leu Asp Leu Gly Gln Val Phe His Val Ala Tyr Val Leu Ile Lys
145                 150                 155                 160
Phe Ala Asn Ser Pro Arg Pro Asp Leu Trp Val Leu Glu Arg Ser Met
                165                 170                 175
Asp Phe Gly Arg Thr Tyr Gln Pro Trp Gln Phe Phe Ala Ser Ser Lys
            180                 185                 190
Arg Asp Cys Leu Glu Arg Phe Gly Pro Gln Thr Leu Glu Arg Ile Thr
        195                 200                 205
Arg Asp Asp Ala Ala Ile Cys Thr Thr Glu Tyr Ser Arg Ile Val Pro
    210                 215                 220
Leu Glu Asn Gly Glu Ile Val Val Ser Leu Val Asn Gly Arg Pro Gly
225                 230                 235                 240
Ala Met Asn Phe Ser Tyr Ser Pro Leu Leu Arg Glu Phe Thr Lys Ala
                245                 250                 255
Thr Asn Val Arg Leu Arg Phe Leu Arg Thr Asn Thr Leu Leu Gly His
            260                 265                 270
Leu Met Gly Lys Ala Leu Arg Asp Pro Thr Val Thr Arg Arg Tyr Tyr
        275                 280                 285
Tyr Ser Ile Lys Asp Ile Ser Ile Gly Gly Arg Cys Val Cys His Gly
    290                 295                 300
His Ala Asp Ala Cys Asp Ala Lys Asp Pro Thr Asp Pro Phe Arg Leu
305                 310                 315                 320
Gln Cys Thr Cys Gln His Asn Thr Cys Gly Gly Thr Cys Asp Arg Cys
                325                 330                 335
Cys Pro Gly Phe Asn Gln Gln Pro Trp Lys Pro Ala Thr Ala Asn Ser
            340                 345                 350
Ala Asn Glu Cys Gln Ser Cys Asn Cys Tyr Gly His Ala Thr Asp Cys
        355                 360                 365
Tyr Tyr Asp Pro Glu Val Asp Arg Arg Arg Ala Ser Gln Ser Leu Asp
    370                 375                 380
Gly Thr Tyr Gln Gly Gly Gly Val Cys Ile Asp Cys Gln His His Thr
385                 390                 395                 400
Thr Gly Val Asn Cys Glu Arg Cys Leu Pro Gly Phe Tyr Arg Ser Pro
                405                 410                 415
Asn His Pro Leu Asp Ser Pro His Val Cys Arg Arg Cys Asn Cys Glu
            420                 425                 430
Ser Asp Phe Thr Asp Gly Thr Cys Glu Asp Leu Thr Gly Arg Cys Tyr
        435                 440                 445
```

```
Cys Arg Pro Asn Phe Ser Gly Glu Arg Cys Asp Val Cys Ala Glu Gly
    450                 455                 460
Phe Thr Gly Phe Pro Ser Cys Tyr Pro Thr Pro Ser Ser Ser Asn Asp
465                 470                 475                 480
Thr Arg Glu Gln Val Leu Pro Ala Gly Gln Ile Val Asn Cys Asp Cys
                485                 490                 495
Ser Ala Ala Gly Thr Gln Gly Asn Ala Cys Arg Lys Asp Pro Arg Val
            500                 505                 510
Gly Arg Cys Leu Cys Lys Pro Asn Phe Gln Gly Thr His Cys Glu Leu
        515                 520                 525
Cys Ala Pro Gly Phe Tyr Gly Pro Gly Cys Gln Pro Cys Gln Cys Ser
    530                 535                 540
Ser Pro Gly Val Ala Asp Asp Arg Cys Asp Pro Asp Thr Gly Gln Cys
545                 550                 555                 560
Arg Cys Arg Val Gly Phe Glu Gly Ala Thr Cys Asp Arg Cys Ala Pro
                565                 570                 575
Gly Tyr Phe His Phe Pro Leu Cys Gln Leu Cys Gly Cys Ser Pro Ala
            580                 585                 590
Gly Thr Leu Pro Glu Gly Cys Asp Glu Ala Gly Arg Cys Leu Cys Gln
        595                 600                 605
Pro Glu Phe Ala Gly Pro His Cys Asp Arg Cys Arg Pro Gly Tyr His
    610                 615                 620
Gly Phe Pro Asn Cys Gln Ala Cys Thr Cys Asp Pro Arg Gly Ala Leu
625                 630                 635                 640
Asp Gln Leu Cys Gly Ala Gly Gly Leu Cys Arg Cys Arg Pro Gly Tyr
                645                 650                 655
Thr Gly Thr Ala Cys Gln Glu Cys Ser Pro Gly Phe His Gly Phe Pro
            660                 665                 670
Ser Cys Val Pro Cys His Cys Ser Ala Glu Gly Ser Leu His Ala Ala
        675                 680                 685
Cys Asp Pro Arg Ser Gly Gln Cys Ser Cys Arg Pro Arg Val Thr Gly
    690                 695                 700
Leu Arg Cys Asp Thr Cys Val Pro Gly Ala Tyr Asn Phe Pro Tyr Cys
705                 710                 715                 720
Glu Ala Gly Ser Cys His Pro Ala Gly Leu Ala Pro Val Asp Pro Ala
                725                 730                 735
Leu Pro Glu Ala Gln Val Pro Cys Met Cys Arg Ala His Val Glu Gly
            740                 745                 750
Pro Ser Cys Asp Arg Cys Lys Pro Gly Phe Trp Gly Leu Ser Pro Ser
        755                 760                 765
Asn Pro Glu Gly Cys Thr Arg Cys Ser Cys Asp Leu Arg Gly Thr Leu
    770                 775                 780
Gly Gly Val Ala Glu Cys Gln Pro Gly Thr Gly Gln Cys Phe Cys Lys
785                 790                 795                 800
Pro His Val Cys Gly Gln Ala Cys Ala Ser Cys Lys Asp Gly Phe Phe
                805                 810                 815
Gly Leu Asp Gln Ala Asp Tyr Phe Gly Cys Arg Ser Cys Arg Cys Asp
            820                 825                 830
Ile Gly Gly Ala Leu Gly Gln Ser Cys Glu Pro Arg Thr Gly Val Cys
        835                 840                 845
Arg Cys Arg Pro Asn Thr Gln Gly Pro Thr Cys Ser Glu Pro Ala Arg
    850                 855                 860
Asp His Tyr Leu Pro Asp Leu His His Leu Arg Leu Glu Leu Glu Glu
865                 870                 875                 880
Ala Ala Thr Pro Glu Gly His Ala Val Arg Phe Gly Phe Asn Pro Leu
                885                 890                 895
Glu Phe Glu Asn Phe Ser Trp Arg Gly Tyr Ala Gln Met Ala Pro Val
            900                 905                 910
Gln Pro Arg Ile Val Ala Arg Leu Asn Leu Thr Ser Pro Asp Leu Phe
```

915 920 925
Trp Leu Val Phe Arg Tyr Val Asn Arg Gly Ala Met Ser Val Ser Gly
930 935 940
Arg Val Ser Val Arg Glu Glu Gly Arg Ser Ala Thr Cys Ala Asn Cys
945 950 955 960
Thr Ala Gln Ser Gln Pro Val Ala Phe Pro Pro Ser Thr Glu Pro Ala
965 970 975
Phe Ile Thr Val Pro Gln Arg Gly Phe Gly Glu Pro Phe Val Leu Asn
980 985 990
Pro Gly Thr Trp Ala Leu Arg Val Glu Ala Glu Gly Val Leu Leu Asp
995 1000 1005
Tyr Val Val Leu Leu Pro Ser Ala Tyr Tyr Glu Ala Ala Leu Leu Gln
1010 1015 1020
Leu Arg Val Thr Glu Ala Cys Thr Tyr Arg Pro Ser Ala Gln Gln Ser
1025 1030 1035 1040
Gly Asp Asn Cys Leu Leu Tyr Thr His Leu Pro Leu Asp Gly Phe Pro
1045 1050 1055
Ser Ala Ala Gly Leu Glu Ala Leu Cys Arg Gln Asp Asn Ser Leu Pro
1060 1065 1070
Arg Pro Cys Pro Thr Glu Gln Leu Ser Pro Ser His Pro Pro Leu Ile
1075 1080 1085
Thr Cys Thr Gly Ser Asp Val Asp Val Gln Leu Gln Val Ala Val Pro
1090 1095 1100
Gln Pro Gly Arg Tyr Ala Leu Val Val Glu Tyr Ala Asn Glu Asp Ala
1105 1110 1115 1120
Arg Gln Glu Val Gly Val Ala Val His Thr Pro Gln Arg Ala Pro Gln
1125 1130 1135
Gln Gly Leu Leu Ser Leu His Pro Cys Leu Tyr Ser Thr Leu Cys Arg
1140 1145 1150
Gly Thr Ala Arg Asp Thr Gln Asp His Leu Ala Val Phe His Leu Asp
1155 1160 1165
Ser Glu Ala Ser Val Arg Leu Thr Ala Glu Gln Ala Arg Phe Phe Leu
1170 1175 1180
His Gly Val Thr Leu Val Pro Ile Glu Glu Phe Ser Pro Glu Phe Val
1185 1190 1195 1200
Glu Pro Arg Val Ser Cys Ile Ser Ser His Gly Ala Phe Gly Pro Asn
1205 1210 1215
Ser Ala Ala Cys Leu Pro Ser Arg Phe Pro Lys Pro Pro Gln Pro Ile
1220 1225 1230
Ile Leu Arg Asp Cys Gln Val Ile Pro Leu Pro Pro Gly Leu Pro Leu
1235 1240 1245
Thr His Ala Gln Asp Leu Thr Pro Ala Met Ser Pro Ala Gly Pro Arg
1250 1255 1260
Pro Arg Pro Pro Thr Ala Val Asp Pro Asp Ala Glu Pro Thr Leu Leu
1265 1270 1275 1280
Arg Glu Pro Gln Ala Thr Val Val Phe Thr Thr His Val Pro Thr Leu
1285 1290 1295
Gly Arg Tyr Ala Phe Leu Leu His Gly Tyr Gln Pro Ala His Pro Thr
1300 1305 1310
Phe Pro Val Glu Val Leu Ile Asn Ala Gly Arg Val Trp Gln Gly His
1315 1320 1325
Ala Asn Ala Ser Phe Cys Pro His Gly Tyr Gly Cys Arg Thr Leu Val
1330 1335 1340
Val Cys Glu Gly Gln Ala Leu Leu Asp Val Thr His Ser Glu Leu Thr
1345 1350 1355 1360
Val Thr Val Arg Val Pro Lys Gly Arg Trp Leu Trp Leu Asp Tyr Val
1365 1370 1375
Leu Val Val Pro Glu Asn Val Tyr Ser Phe Gly Tyr Leu Arg Glu Glu
1380 1385 1390

Pro Leu Asp Lys Ser Tyr Asp Phe Ile Ser His Cys Ala Ala Gln Gly
1395 1400 1405
Tyr His Ile Ser Pro Ser Ser Ser Ser Leu Phe Cys Arg Asn Ala Ala
1410 1415 1420
Ala Ser Leu Ser Leu Phe Tyr Asn Asn Gly Ala Arg Pro Cys Gly Cys
1425 1430 1435 1440
His Glu Val Gly Ala Thr Gly Pro Thr Cys Glu Pro Phe Gly Gly Gln
1445 1450 1455
Cys Pro Cys His Ala His Val Ile Gly Arg Asp Cys Ser Arg Cys Ala
1460 1465 1470
Thr Gly Tyr Trp Gly Phe Pro Asn Cys Arg Pro Cys Asp Cys Gly Ala
1475 1480 1485
Arg Leu Cys Asp Glu Leu Thr Gly Gln Cys Ile Cys Pro Pro Arg Thr
1490 1495 1500
Ile Pro Pro Asp Cys Leu Leu Cys Gln Pro Gln Thr Phe Gly Cys His
1505 1510 1515 1520
Pro Leu Val Gly Cys Glu Glu Cys Asn Cys Ser Gly Pro Gly Ile Gln
1525 1530 1535
Glu Leu Thr Asp Pro Thr Cys Asp Thr Asp Ser Gly Gln Cys Lys Cys
1540 1545 1550
Arg Pro Asn Val Thr Gly Arg Arg Cys Asp Thr Cys Ser Pro Gly Phe
1555 1560 1565
His Gly Tyr Pro Arg Cys Arg Pro Cys Asp Cys His Glu Ala Gly Thr
1570 1575 1580
Ala Pro Gly Val Cys Asp Pro Leu Thr Gly Gln Cys Tyr Cys Lys Glu
1585 1590 1595 1600
Asn Val Gln Gly Pro Lys Cys Asp Gln Cys Ser Leu Gly Thr Phe Ser
1605 1610 1615
Leu Asp Ala Ala Asn Pro Lys Gly Cys Thr Arg Cys Phe Cys Phe Gly
1620 1625 1630
Ala Thr Glu Arg Cys Arg Ser Ser Ser Tyr Thr Arg Gln Glu Phe Val
1635 1640 1645
Asp Met Glu Gly Trp Val Leu Leu Ser Thr Asp Arg Gln Val Val Pro
1650 1655 1660
His Glu Arg Gln Pro Gly Thr Glu Met Leu Arg Ala Asp Leu Arg His
1665 1670 1675 1680
Val Pro Glu Ala Val Pro Glu Ala Phe Pro Glu Leu Tyr Trp Gln Ala
1685 1690 1695
Pro Pro Ser Tyr Leu Gly Asp Arg Val Ser Ser Tyr Gly Gly Thr Leu
1700 1705 1710
Arg Tyr Glu Leu His Ser Glu Thr Gln Arg Gly Asp Val Phe Val Pro
1715 1720 1725
Met Glu Ser Arg Pro Asp Val Val Leu Gln Gly Asn Gln Met Ser Ile
1730 1735 1740
Thr Phe Leu Glu Pro Ala Tyr Pro Thr Pro Gly His Val His Arg Gly
1745 1750 1755 1760
Gln Leu Gln Leu Val Glu Gly Asn Phe Arg His Thr Glu Thr Arg Asn
1765 1770 1775
Thr Val Ser Arg Glu Glu Leu Met Met Val Leu Ala Ser Leu Glu Gln
1780 1785 1790
Leu Gln Ile Arg Ala Leu Phe Ser Gln Ile Ser Ser Ala Val Phe Leu
1795 1800 1805
Arg Arg Val Ala Leu Glu Val Ala Ser Pro Ala Gly Gln Gly Ala Leu
1810 1815 1820
Ala Ser Asn Val Glu Leu Cys Leu Cys Pro Ala Ser Tyr Arg Gly Asp
1825 1830 1835 1840
Ser Cys Gln Glu Cys Ala Pro Gly Phe Tyr Arg Asp Val Lys Gly Leu
1845 1850 1855
Phe Leu Gly Arg Cys Val Pro Cys Gln Cys His Gly His Ser Asp Arg

1860 1865 1870
Cys Leu Pro Gly Ser Gly Val Cys Val Asp Cys Gln His Asn Thr Glu
1875 1880 1885
Gly Ala His Cys Glu Arg Cys Gln Ala Gly Phe Val Ser Ser Arg Asp
1890 1895 1900
Asp Pro Ser Ala Pro Cys Val Ser Cys Pro Cys Pro Leu Ser Val Pro
1905 1910 1915 1920
Ser Asn Asn Phe Ala Glu Gly Cys Val Leu Arg Gly Gly Arg Thr Gln
1925 1930 1935
Cys Leu Cys Lys Pro Gly Tyr Ala Gly Ala Ser Cys Glu Arg Cys Ala
1940 1945 1950
Pro Gly Phe Phe Gly Asn Pro Leu Val Leu Gly Ser Ser Cys Gln Pro
1955 1960 1965
Cys Asp Cys Ser Gly Asn Gly Asp Pro Asn Leu Leu Phe Ser Asp Cys
1970 1975 1980
Asp Pro Leu Thr Gly Ala Cys Arg Gly Cys Leu Arg His Thr Thr Gly
1985 1990 1995 2000
Pro Arg Cys Glu Ile Cys Ala Pro Gly Phe Tyr Gly Asn Ala Leu Leu
2005 2010 2015
Pro Gly Asn Cys Thr Arg Cys Asp Cys Thr Pro Cys Gly Thr Glu Ala
2020 2025 2030
Cys Asp Pro His Ser Gly His Cys Leu Cys Lys Ala Gly Val Thr Gly
2035 2040 2045
Arg Arg Cys Asp Arg Cys Gln Glu Gly His Phe Gly Phe Asp Gly Cys
2050 2055 2060
Gly Gly Cys Arg Pro Cys Ala Cys Gly Pro Ala Ala Glu Gly Ser Glu
2065 2070 2075 2080
Cys His Pro Gln Ser Gly Gln Cys His Cys Arg Pro Gly Thr Met Gly
2085 2090 2095
Pro Gln Cys Arg Glu Cys Ala Pro Gly Tyr Trp Gly Leu Pro Glu Gln
2100 2105 2110
Gly Cys Arg Arg Cys Gln Cys Pro Gly Gly Arg Cys Asp Pro His Thr
2115 2120 2125
Gly Arg Cys Asn Cys Pro Pro Gly Leu Ser Gly Glu Arg Cys Asp Thr
2130 2135 2140
Cys Ser Gln Gln His Gln Val Pro Val Pro Gly Gly Pro Val Gly His
2145 2150 2155 2160
Ser Ile His Cys Glu Val Cys Asp His Cys Val Val Leu Leu Leu Asp
2165 2170 2175
Asp Leu Glu Arg Ala Gly Ala Leu Leu Pro Ala Ile His Glu Gln Leu
2180 2185 2190
Arg Gly Ile Asn Ala Ser Ser Met Ala Trp Ala Arg Leu His Arg Leu
2195 2200 2205
Asn Ala Ser Ile Ala Asp Leu Gln Ser Gln Leu Arg Ser Pro Leu Gly
2210 2215 2220
Pro Arg His Glu Thr Ala Gln Gln Leu Glu Val Leu Glu Gln Gln Ser
2225 2230 2235 2240
Thr Ser Leu Gly Gln Asp Ala Arg Arg Leu Gly Gly Gln Ala Gly Ala
2245 2250 2255
Pro Arg Pro Pro Arg Ala Pro Gly Gly Phe His Leu Tyr Gln Ala Ser
2260 2265 2270
Gln Leu Leu Ala Gly Thr Glu Ala Thr Leu Gly His Ala Lys Thr Leu
2275 2280 2285
Leu Ala Ala Ile Arg Ala Val Asp Arg Thr Leu Ser Glu Leu Met Ser
2290 2295 2300
Gln Thr Gly His Leu Gly Leu Ala Asn Ala Ser Ala Pro Ser Gly Glu
2305 2310 2315 2320
Gln Leu Leu Arg Thr Leu Ala Glu Val Glu Arg Leu Leu Trp Glu Met
2325 2330 2335

Arg Ala Arg Asp Leu Gly Ala Pro Gln Ala Ala Ala Glu Ala Glu Leu
2340 2345 2350
Ala Ala Ala Gln Arg Leu Leu Ala Arg Val Gln Glu Gln Leu Ser Ser
2355 2360 2365
Leu Trp Glu Glu Asn Gln Ala Leu Ala Thr Gln Thr Arg Asp Arg Leu
2370 2375 2380
Ala Gln His Glu Ala Gly Leu Met Asp Leu Arg Glu Ala Leu Asn Arg
2385 2390 2395 2400
Ala Val Asp Ala Thr Arg Glu Ala Gln Glu Leu Asn Ser Arg Asn Gln
2405 2410 2415
Glu Arg Leu Glu Glu Ala Leu Gln Arg Lys Gln Glu Leu Ser Arg Asp
2420 2425 2430
Asn Ala Thr Leu Gln Ala Thr Leu His Ala Ala Arg Asp Thr Leu Ala
2435 2440 2445
Ser Val Phe Arg Leu Leu His Ser Leu Asp Gln Ala Lys Glu Glu Leu
2450 2455 2460
Glu Arg Leu Ala Ala Ser Leu Asp Gly Ala Arg Thr Pro Leu Leu Gln
2465 2470 2475 2480
Arg Met Gln Thr Phe Ser Pro Ala Gly Ser Lys Leu Arg Leu Val Glu
2485 2490 2495
Ala Ala Glu Ala His Ala Gln Gln Leu Gly Gln Leu Ala Leu Asn Leu
2500 2505 2510
Ser Ser Ile Ile Leu Asp Val Asn Gln Asp Arg Leu Thr Gln Arg Ala
2515 2520 2525
Ile Glu Ala Ser Asn Ala Tyr Ser Arg Ile Leu Gln Ala Val Gln Ala
2530 2535 2540
Ala Glu Asp Ala Ala Gly Gln Ala Leu Gln Gln Ala Asp His Thr Trp
2545 2550 2555 2560
Ala Thr Val Val Arg Gln Gly Leu Val Asp Arg Ala Gln Gln Leu Leu
2565 2570 2575
Ala Asn Ser Thr Ala Leu Glu Glu Ala Met Leu Gln Glu Gln Gln Arg
2580 2585 2590
Leu Gly Leu Val Trp Ala Ala Leu Gln Gly Ala Arg Thr Gln Leu Arg
2595 2600 2605
Asp Val Arg Ala Lys Lys Asp Gln Leu Glu Ala His Ile Gln Ala Ala
2610 2615 2620
Gln Ala Met Leu Ala Met Asp Thr Asp Glu Thr Ser Lys Lys Ile Ala
2625 2630 2635 2640
His Ala Lys Ala Val Ala Ala Glu Ala Gln Asp Thr Ala Thr Arg Val
2645 2650 2655
Gln Ser Gln Leu Gln Ala Met Gln Glu Asn Val Glu Arg Trp Gln Gly
2660 2665 2670
Gln Tyr Glu Gly Leu Arg Gly Gln Asp Leu Gly Gln Ala Val Leu Asp
2675 2680 2685
Ala Gly His Ser Val Ser Thr Leu Glu Lys Thr Leu Pro Gln Leu Leu
2690 2695 2700
Ala Lys Leu Ser Ile Leu Glu Asn Arg Gly Val His Asn Ala Ser Leu
2705 2710 2715 2720
Ala Leu Ser Ala Ser Ile Gly Arg Val Arg Glu Leu Ile Ala Gln Ala
2725 2730 2735
Arg Gly Ala Ala Ser Lys Val Lys Val Pro Met Lys Phe Asn Gly Arg
2740 2745 2750
Ser Gly Val Gln Leu Arg Thr Pro Arg Asp Leu Ala Asp Leu Ala Ala
2755 2760 2765
Tyr Thr Ala Leu Lys Phe Tyr Leu Gln Gly Pro Glu Pro Glu Pro Gly
2770 2775 2780
Gln Gly Thr Glu Asp Arg Phe Val Met Tyr Met Gly Ser Arg Gln Ala
2785 2790 2795 2800
Thr Gly Asp Tyr Met Gly Val Ser Leu Arg Asp Lys Lys Val His Trp

2805 2810 2815
Val Tyr Gln Leu Gly Glu Ala Gly Pro Ala Val Leu Ser Ile Asp Glu
2820 2825 2830
Asp Ile Gly Glu Gln Phe Ala Ala Val Ser Leu Asp Arg Thr Leu Gln
2835 2840 2845
Phe Gly His Met Ser Val Thr Val Glu Arg Gln Met Ile Gln Glu Thr
2850 2855 2860
Lys Gly Asp Thr Val Ala Pro Gly Ala Glu Gly Leu Leu Asn Leu Arg
2865 2870 2875 2880
Pro Asp Asp Phe Val Phe Tyr Val Gly Gly Tyr Pro Ser Thr Phe Thr
2885 2890 2895
Pro Pro Pro Leu Leu Arg Phe Pro Gly Tyr Arg Gly Cys Ile Glu Met
2900 2905 2910
Asp Thr Leu Asn Glu Glu Val Val Ser Leu Tyr Asn Phe Glu Arg Thr
2915 2920 2925
Phe Gln Leu Asp Thr Ala Val Asp Arg Pro Cys Ala Arg Ser Lys Ser
2930 2935 2940
Thr Gly Asp Pro Trp Leu Thr Asp Gly Ser Tyr Leu Asp Gly Thr Gly
2945 2950 2955 2960
Phe Ala Arg Ile Ser Phe Asp Ser Gln Ile Ser Thr Thr Lys Arg Phe
2965 2970 2975
Glu Gln Glu Leu Arg Leu Val Ser Tyr Ser Gly Val Leu Phe Phe Leu
2980 2985 2990
Lys Gln Gln Ser Gln Phe Leu Cys Leu Ala Val Gln Glu Gly Ser Leu
2995 3000 3005
Val Leu Leu Tyr Asp Phe Gly Ala Gly Leu Lys Lys Ala Val Pro Leu
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Gln Pro Pro Pro Pro Leu Thr Ser Ala Ser Lys Ala Ile Gln Val Phe
3025 3030 3035 3040
Leu Leu Gly Gly Ser Arg Lys Arg Val Leu Val Arg Val Glu Arg Ala
3045 3050 3055
Thr Val Tyr Ser Val Glu Gln Asp Asn Asp Leu Glu Leu Ala Asp Ala
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Tyr Tyr Leu Gly Gly Val Pro Pro Asp Gln Leu Pro Pro Ser Leu Arg
3075 3080 3085
Arg Leu Phe Pro Thr Gly Gly Ser Val Arg Gly Cys Val Lys Gly Ile
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Lys Ala Leu Gly Lys Tyr Val Asp Leu Lys Arg Leu Asn Thr Thr Gly
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Phe His Gly His Gly Phe Leu Arg Leu Ala Leu Ser Asn Val Ala Pro
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Leu Thr Gly Asn Val Tyr Ser Gly Phe Gly Phe His Ser Ala Gln Asp
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Ser Ala Leu Leu Tyr Tyr Arg Ala Ser Pro Asp Gly Leu Cys Gln Val
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Ser Leu Gln Gln Gly Arg Val Ser Leu Gln Leu Leu Arg Thr Glu Val
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Lys Thr Gln Ala Gly Phe Ala Asp Gly Ala Pro His Tyr Val Ala Phe
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Tyr Ser Asn Ala Thr Gly Val Trp Leu Tyr Val Asp Asp Gln Leu Gln
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Gln Met Lys Pro His Arg Gly Pro Pro Pro Glu Leu Gln Pro Gln Pro
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Glu Gly Pro Pro Arg Leu Leu Leu Gly Gly Leu Pro Glu Ser Gly Thr
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Ile Tyr Asn Phe Ser Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu
3265 3270 3275 3280

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Asn Val Ser Thr Gly Cys Ala Pro Ala Leu Gln Ala Gln Thr Pro Gly
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Leu Gly Pro Arg Gly Leu Gln Ala Thr Ala Arg Lys Ala Ser Arg Arg
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Ser Arg Gln Pro Ala Arg His Pro Ala Cys Met Leu Pro Pro His Leu
    3330                3335                3340
Arg Thr Thr Arg Asp Ser Tyr Gln Phe Gly Gly Ser Leu Ser Ser His
3345                3350                3355                3360
Leu Glu Phe Val Gly Ile Leu Ala Arg His Arg Asn Trp Pro Ser Leu
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Ser Met His Val Leu Pro Arg Ser Ser Arg Gly Leu Leu Leu Phe Thr
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Ala Arg Leu Arg Pro Gly Ser Pro Ser Leu Ala Leu Phe Leu Ser Asn
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Gly His Phe Val Ala Gln Met Glu Gly Leu Gly Thr Arg Leu Arg Ala
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Gln Ser Arg Gln Arg Ser Arg Pro Gly Arg Trp His Lys Val Ser Val
3425                3430                3435                3440
Arg Trp Glu Lys Asn Arg Ile Leu Leu Val Thr Asp Gly Ala Arg Ala
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Trp Ser Gln Glu Gly Pro His Arg Gln His Gln Gly Ala Glu His Pro
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Gln Pro His Thr Leu Phe Val Gly Gly Leu Pro Ala Ser Ser His Ser
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Ser Lys Leu Pro Val Thr Val Gly Phe Ser Gly Cys Val Lys Arg Leu
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Arg Leu His Gly Arg Pro Leu Gly Ala Pro Thr Arg Met Ala Gly Val
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Thr Pro Cys Ile Leu Gly Pro Leu Glu Ala Gly Leu Phe Phe Pro Gly
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Ser Gly Gly Val Ile Thr Leu Asp Leu Pro Gly Ala Thr Leu Pro Asp
            3540                3545                3550
Val Gly Leu Glu Leu Glu Val Arg Pro Leu Ala Val Thr Gly Leu Ile
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Phe His Leu Gly Gln Ala Arg Thr Pro Pro Tyr Leu Gln Leu Gln Val
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Thr Glu Lys Gln Val Leu Leu Arg Ala Asp Asp Gly Ala Gly Glu Phe
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Ser Thr Ser Val Thr Arg Pro Ser Val Leu Cys Asp Gly Gln Trp His
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Arg Leu Ala Val Met Lys Ser Gly Asn Val Leu Arg Leu Glu Val Asp
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Ala Gln Ser Asn His Thr Val Gly Pro Leu Leu Ala Ala Ala Ala Gly
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Ala Pro Ala Pro Leu Tyr Leu Gly Gly Leu Pro Glu Pro Met Ala Val
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Gln Pro Trp Pro Pro Ala Tyr Cys Gly Cys Met Arg Arg Leu Ala Val
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Asn Arg Ser Pro Val Ala Met Thr Arg Ser Val Glu Val His Gly Ala
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Val Gly Ala Ser Gly Cys Pro Ala Ala
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<211> 3696
<212> PRT

<213> Homo sapiens

<400> 31

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Arg Gly Pro Ala Pro Leu Leu Leu Val Gly Leu Ala Leu Leu Gly Ala
            20                  25                  30
Ala Arg Ala Arg Glu Glu Ala Gly Gly Gly Phe Ser Leu His Pro Pro
        35                  40                  45
Tyr Phe Asn Leu Ala Glu Gly Ala Arg Ile Ala Ala Ser Ala Thr Cys
    50                  55                  60
Gly Glu Glu Ala Pro Ala Arg Gly Ser Pro Arg Pro Thr Glu Asp Leu
65                  70                  75                  80
Tyr Cys Lys Leu Val Gly Gly Pro Val Ala Gly Gly Asp Pro Asn Gln
                85                  90                  95
Thr Ile Arg Gly Gln Tyr Cys Asp Ile Cys Thr Ala Ala Asn Ser Asn
            100                 105                 110
Lys Ala His Pro Ala Ser Asn Ala Ile Asp Gly Thr Glu Arg Trp Trp
        115                 120                 125
Gln Ser Pro Pro Leu Ser Arg Gly Leu Glu Tyr Asn Glu Val Asn Val
    130                 135                 140
Thr Leu Asp Leu Gly Gln Val Phe His Val Ala Tyr Val Leu Ile Lys
145                 150                 155                 160
Phe Ala Asn Ser Pro Arg Pro Asp Leu Trp Val Leu Glu Arg Ser Met
                165                 170                 175
Asp Phe Gly Arg Thr Tyr Gln Pro Trp Gln Phe Phe Ala Ser Ser Lys
            180                 185                 190
Arg Asp Cys Leu Glu Arg Phe Gly Pro Gln Thr Leu Glu Arg Ile Thr
        195                 200                 205
Arg Asp Asp Ala Ala Ile Cys Thr Thr Glu Tyr Ser Arg Ile Val Pro
    210                 215                 220
Leu Glu Asn Gly Glu Ile Val Val Ser Leu Val Asn Gly Arg Pro Gly
225                 230                 235                 240
Ala Met Asn Phe Ser Tyr Ser Pro Leu Leu Arg Glu Phe Thr Lys Ala
                245                 250                 255
Thr Asn Val Arg Leu Arg Phe Leu Arg Thr Asn Thr Leu Leu Gly His
            260                 265                 270
Leu Met Gly Lys Ala Leu Arg Asp Pro Thr Val Thr Arg Arg Tyr Tyr
        275                 280                 285
Tyr Ser Ile Lys Asp Ile Ser Ile Gly Gly Arg Cys Val Cys His Gly
    290                 295                 300
His Ala Asp Ala Cys Asp Ala Lys Asp Pro Thr Asp Pro Phe Arg Leu
305                 310                 315                 320
Gln Cys Thr Cys Gln His Asn Thr Cys Gly Gly Thr Cys Asp Arg Cys
                325                 330                 335
Cys Pro Gly Phe Asn Gln Gln Pro Trp Lys Pro Ala Thr Ala Asn Ser
            340                 345                 350
Ala Asn Glu Cys Gln Ser Cys Asn Cys Tyr Gly His Ala Thr Asp Cys
        355                 360                 365
Tyr Tyr Asp Pro Glu Val Asp Arg Arg Arg Ala Ser Gln Ser Leu Asp
    370                 375                 380
Gly Thr Tyr Gln Gly Gly Gly Val Cys Ile Asp Cys Gln His His Thr
385                 390                 395                 400
Thr Gly Val Asn Cys Glu Arg Cys Leu Pro Gly Phe Tyr Arg Ser Pro
                405                 410                 415
Asn His Pro Leu Asp Ser Pro His Val Cys Arg Arg Cys Asn Cys Glu
            420                 425                 430
Ser Asp Phe Thr Asp Gly Thr Cys Glu Asp Leu Thr Gly Arg Cys Tyr
        435                 440                 445
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Cys Arg Pro Asn Phe Ser Gly Glu Arg Cys Asp Val Cys Ala Glu Gly
    450                 455                 460
Phe Thr Gly Phe Pro Ser Cys Tyr Pro Thr Pro Ser Ser Ser Asn Asp
465                 470                 475                 480
Thr Arg Glu Gln Val Leu Pro Ala Gly Gln Ile Val Asn Cys Asp Cys
                485                 490                 495
Ser Ala Ala Gly Thr Gln Gly Asn Ala Cys Arg Lys Asp Pro Arg Val
            500                 505                 510
Gly Arg Cys Leu Cys Lys Pro Asn Phe Gln Gly Thr His Cys Glu Leu
        515                 520                 525
Cys Ala Pro Gly Phe Tyr Gly Pro Gly Cys Gln Pro Cys Gln Cys Ser
    530                 535                 540
Ser Pro Gly Val Ala Asp Asp Arg Cys Asp Pro Asp Thr Gly Gln Cys
545                 550                 555                 560
Arg Cys Arg Val Gly Phe Glu Gly Ala Thr Cys Asp Arg Cys Ala Pro
                565                 570                 575
Gly Tyr Phe His Phe Pro Leu Cys Gln Leu Cys Gly Cys Ser Pro Ala
            580                 585                 590
Gly Thr Leu Pro Glu Gly Cys Asp Glu Ala Gly Arg Cys Leu Cys Gln
        595                 600                 605
Pro Glu Phe Ala Gly Pro His Cys Asp Arg Cys Arg Pro Gly Tyr His
    610                 615                 620
Gly Phe Pro Asn Cys Gln Ala Cys Thr Cys Asp Pro Arg Gly Ala Leu
625                 630                 635                 640
Asp Gln Leu Cys Gly Ala Gly Gly Leu Cys Arg Cys Arg Pro Gly Tyr
                645                 650                 655
Thr Gly Thr Ala Cys Gln Glu Cys Ser Pro Gly Phe His Gly Phe Pro
            660                 665                 670
Ser Cys Val Pro Cys His Cys Ser Ala Glu Gly Ser Leu His Ala Ala
        675                 680                 685
Cys Asp Pro Arg Ser Gly Gln Cys Ser Cys Arg Pro Arg Val Thr Gly
    690                 695                 700
Leu Arg Cys Asp Thr Cys Val Pro Gly Ala Tyr Asn Phe Pro Tyr Cys
705                 710                 715                 720
Glu Ala Gly Ser Cys His Pro Ala Gly Leu Ala Pro Val Asp Pro Ala
                725                 730                 735
Leu Pro Glu Ala Gln Val Pro Cys Met Cys Arg Ala His Val Glu Gly
            740                 745                 750
Pro Ser Cys Asp Arg Cys Lys Pro Gly Phe Trp Gly Leu Ser Pro Ser
        755                 760                 765
Asn Pro Glu Gly Cys Thr Arg Cys Ser Cys Asp Leu Arg Gly Thr Leu
    770                 775                 780
Gly Gly Val Ala Glu Cys Gln Pro Gly Thr Gly Gln Cys Phe Cys Lys
785                 790                 795                 800
Pro His Val Cys Gly Gln Ala Cys Ala Ser Cys Lys Asp Gly Phe Phe
                805                 810                 815
Gly Leu Asp Gln Ala Asp Tyr Phe Gly Cys Arg Ser Cys Arg Cys Asp
            820                 825                 830
Ile Gly Gly Ala Leu Gly Gln Ser Cys Glu Pro Arg Thr Gly Val Cys
        835                 840                 845
Arg Cys Arg Pro Asn Thr Gln Gly Pro Thr Cys Ser Glu Pro Ala Arg
    850                 855                 860
Asp His Tyr Leu Pro Asp Leu His His Leu Arg Leu Glu Leu Glu Glu
865                 870                 875                 880
Ala Ala Thr Pro Glu Gly His Ala Val Arg Phe Gly Phe Asn Pro Leu
                885                 890                 895
Glu Phe Glu Asn Phe Ser Trp Arg Gly Tyr Ala Gln Met Ala Pro Val
            900                 905                 910
Gln Pro Arg Ile Val Ala Arg Leu Asn Leu Thr Ser Pro Asp Leu Phe
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915 920 925
Trp Leu Val Phe Arg Tyr Val Asn Arg Gly Ala Met Ser Val Ser Gly
930 935 940
Arg Val Ser Val Arg Glu Glu Gly Arg Ser Ala Thr Cys Ala Asn Cys
945 950 955 960
Thr Ala Gln Ser Gln Pro Val Ala Phe Pro Pro Ser Thr Glu Pro Ala
965 970 975
Phe Ile Thr Val Pro Gln Arg Gly Phe Gly Glu Pro Phe Val Leu Asn
980 985 990
Pro Gly Thr Trp Ala Leu Arg Val Glu Ala Glu Gly Val Leu Leu Asp
995 1000 1005
Tyr Val Val Leu Leu Pro Ser Ala Tyr Tyr Glu Ala Ala Leu Leu Gln
1010 1015 1020
Leu Arg Val Thr Glu Ala Cys Thr Tyr Arg Pro Ser Ala Gln Gln Ser
1025 1030 1035 1040
Gly Asp Asn Cys Leu Leu Tyr Thr His Leu Pro Leu Asp Gly Phe Pro
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Ser Ala Ala Gly Leu Glu Ala Leu Cys Arg Gln Asp Asn Ser Leu Pro
1060 1065 1070
Arg Pro Cys Pro Thr Glu Gln Leu Ser Pro Ser His Pro Pro Leu Ile
1075 1080 1085
Thr Cys Thr Gly Ser Asp Val Asp Val Gln Leu Gln Val Ala Val Pro
1090 1095 1100
Gln Pro Gly Arg Tyr Ala Leu Val Val Glu Tyr Ala Asn Glu Asp Ala
1105 1110 1115 1120
Arg Gln Glu Val Gly Val Ala Val His Thr Pro Gln Arg Ala Pro Gln
1125 1130 1135
Gln Gly Leu Leu Ser Leu His Pro Cys Leu Tyr Ser Thr Leu Cys Arg
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Gly Thr Ala Arg Asp Thr Gln Asp His Leu Ala Val Phe His Leu Asp
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Ser Glu Ala Ser Val Arg Leu Thr Ala Glu Gln Ala Arg Phe Phe Leu
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His Gly Val Thr Leu Val Pro Ile Glu Glu Phe Ser Pro Glu Phe Val
1185 1190 1195 1200
Glu Pro Arg Val Ser Cys Ile Ser Ser His Gly Ala Phe Gly Pro Asn
1205 1210 1215
Ser Ala Ala Cys Leu Pro Ser Arg Phe Pro Lys Pro Pro Gln Pro Ile
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Ile Leu Arg Asp Cys Gln Val Ile Pro Leu Pro Pro Gly Leu Pro Leu
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Thr His Ala Gln Asp Leu Thr Pro Ala Met Ser Pro Ala Gly Pro Arg
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Pro Arg Pro Pro Thr Ala Val Asp Pro Asp Ala Glu Pro Thr Leu Leu
1265 1270 1275 1280
Arg Glu Pro Gln Ala Thr Val Val Phe Thr Thr His Val Pro Thr Leu
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Gly Arg Tyr Ala Phe Leu Leu His Gly Tyr Gln Pro Ala His Pro Thr
1300 1305 1310
Phe Pro Val Glu Val Leu Ile Asn Ala Gly Arg Val Trp Gln Gly His
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Ala Asn Ala Ser Phe Cys Pro His Gly Tyr Gly Cys Arg Thr Leu Val
1330 1335 1340
Val Cys Glu Gly Gln Ala Leu Leu Asp Val Thr His Ser Glu Leu Thr
1345 1350 1355 1360
Val Thr Val Arg Val Pro Lys Gly Arg Trp Leu Trp Leu Asp Tyr Val
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Leu Val Val Pro Glu Asn Val Tyr Ser Phe Gly Tyr Leu Arg Glu Glu
1380 1385 1390

Pro Leu Asp Lys Ser Tyr Asp Phe Ile Ser His Cys Ala Ala Gln Gly
1395 1400 1405
Tyr His Ile Ser Pro Ser Ser Ser Ser Leu Phe Cys Arg Asn Ala Ala
1410 1415 1420
Ala Ser Leu Ser Leu Phe Tyr Asn Asn Gly Ala Arg Pro Cys Gly Cys
1425 1430 1435 1440
His Glu Val Gly Ala Thr Gly Pro Thr Cys Glu Pro Phe Gly Gly Gln
1445 1450 1455
Cys Pro Cys His Ala His Val Ile Gly Arg Asp Cys Ser Arg Cys Ala
1460 1465 1470
Thr Gly Tyr Trp Gly Phe Pro Asn Cys Arg Pro Cys Asp Cys Gly Ala
1475 1480 1485
Arg Leu Cys Asp Glu Leu Thr Gly Gln Cys Ile Cys Pro Pro Arg Thr
1490 1495 1500
Ile Pro Pro Asp Cys Leu Leu Cys Gln Pro Gln Thr Phe Gly Cys His
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Pro Leu Val Gly Cys Glu Glu Cys Asn Cys Ser Gly Pro Gly Ile Gln
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Glu Leu Thr Asp Pro Thr Cys Asp Thr Asp Ser Gly Gln Cys Lys Cys
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Arg Pro Asn Val Thr Gly Arg Arg Cys Asp Thr Cys Ser Pro Gly Phe
1555 1560 1565
His Gly Tyr Pro Arg Cys Arg Pro Cys Asp Cys His Glu Ala Gly Thr
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Ala Pro Gly Val Cys Asp Pro Leu Thr Gly Gln Cys Tyr Cys Lys Glu
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Asn Val Gln Gly Pro Lys Cys Asp Gln Cys Ser Leu Gly Thr Phe Ser
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Leu Asp Ala Ala Asn Pro Lys Gly Cys Thr Arg Cys Phe Cys Phe Gly
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Ala Thr Glu Arg Cys Arg Ser Ser Ser Tyr Thr Arg Gln Glu Phe Val
1635 1640 1645
Asp Met Glu Gly Trp Val Leu Leu Ser Thr Asp Arg Gln Val Val Pro
1650 1655 1660
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Val Pro Glu Ala Val Pro Glu Ala Phe Pro Glu Leu Tyr Trp Gln Ala
1685 1690 1695
Pro Pro Ser Tyr Leu Gly Asp Arg Val Ser Ser Tyr Gly Gly Thr Leu
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Arg Tyr Glu Leu His Ser Glu Thr Gln Arg Gly Asp Val Phe Val Pro
1715 1720 1725
Met Glu Ser Arg Pro Asp Val Val Leu Gln Gly Asn Gln Met Ser Ile
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Thr Phe Leu Glu Pro Ala Tyr Pro Thr Pro Gly His Val His Arg Gly
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Gln Leu Gln Leu Val Glu Gly Asn Phe Arg His Thr Glu Thr Arg Asn
1765 1770 1775
Thr Val Ser Arg Glu Glu Leu Met Met Val Leu Ala Ser Leu Glu Gln
1780 1785 1790
Leu Gln Ile Arg Ala Leu Phe Ser Gln Ile Ser Ser Ala Val Phe Leu
1795 1800 1805
Arg Arg Val Ala Leu Glu Val Ala Ser Pro Ala Gly Gln Gly Ala Leu
1810 1815 1820
Ala Ser Asn Val Glu Leu Cys Leu Cys Pro Ala Ser Tyr Arg Gly Asp
1825 1830 1835 1840
Ser Cys Gln Glu Cys Ala Pro Gly Phe Tyr Arg Asp Val Lys Gly Leu
1845 1850 1855
Phe Leu Gly Arg Cys Val Pro Cys Gln Cys His Gly His Ser Asp Arg

1860 1865 1870
Cys Leu Pro Gly Ser Gly Val Cys Val Asp Cys Gln His Asn Thr Glu
1875 1880 1885
Gly Ala His Cys Glu Arg Cys Gln Ala Gly Phe Val Ser Ser Arg Asp
1890 1895 1900
Asp Pro Ser Ala Pro Cys Val Ser Cys Pro Cys Pro Leu Ser Val Pro
1905 1910 1915 1920
Ser Asn Asn Phe Ala Glu Gly Cys Val Leu Arg Gly Gly Arg Thr Gln
1925 1930 1935
Cys Leu Cys Lys Pro Gly Tyr Ala Gly Ala Ser Cys Glu Arg Cys Ala
1940 1945 1950
Pro Gly Phe Phe Gly Asn Pro Leu Val Leu Gly Ser Ser Cys Gln Pro
1955 1960 1965
Cys Asp Cys Ser Gly Asn Gly Asp Pro Asn Leu Leu Phe Ser Asp Cys
1970 1975 1980
Asp Pro Leu Thr Gly Ala Cys Arg Gly Cys Leu Arg His Thr Thr Gly
1985 1990 1995 2000
Pro Arg Cys Glu Ile Cys Ala Pro Gly Phe Tyr Gly Asn Ala Leu Leu
2005 2010 2015
Pro Gly Asn Cys Thr Arg Cys Asp Cys Thr Pro Cys Gly Thr Glu Ala
2020 2025 2030
Cys Asp Pro His Ser Gly His Cys Leu Cys Lys Ala Gly Val Thr Gly
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Arg Arg Cys Asp Arg Cys Gln Glu Gly His Phe Gly Phe Asp Gly Cys
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Cys His Pro Gln Ser Gly Gln Cys His Cys Arg Pro Gly Thr Met Gly
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Pro Gln Cys Arg Glu Cys Ala Pro Gly Tyr Trp Gly Leu Pro Glu Gln
2100 2105 2110
Gly Cys Arg Arg Cys Gln Cys Pro Gly Gly Arg Cys Asp Pro His Thr
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Gly Arg Cys Asn Cys Pro Pro Gly Leu Ser Gly Glu Arg Cys Asp Thr
2130 2135 2140
Cys Ser Gln Gln His Gln Val Pro Val Pro Gly Gly Pro Val Gly His
2145 2150 2155 2160
Ser Ile His Cys Glu Val Cys Asp His Cys Val Val Leu Leu Leu Asp
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Asp Leu Glu Arg Ala Gly Ala Leu Leu Pro Ala Ile His Glu Gln Leu
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Arg Gly Ile Asn Ala Ser Ser Met Ala Trp Ala Arg Leu His Arg Leu
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Asn Ala Ser Ile Ala Asp Leu Gln Ser Gln Leu Arg Ser Pro Leu Gly
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Pro Arg His Glu Thr Ala Gln Gln Leu Glu Val Leu Glu Gln Gln Ser
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Thr Ser Leu Gly Gln Asp Ala Arg Arg Leu Gly Gly Gln Ala Ala Val
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Gly Thr Arg Asp Gln Ala Ser Gln Leu Leu Ala Gly Thr Glu Ala Thr
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Leu Gly His Ala Lys Thr Leu Leu Ala Ala Ile Arg Ala Val Asp Arg
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Glu Arg Leu Leu Trp Glu Met Arg Ala Arg Asp Leu Gly Ala Pro Gln
2325 2330 2335

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Val Gln Glu Gln Leu Ser Ser Leu Trp Glu Glu Asn Gln Ala Leu Ala
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Lys Gln Glu Leu Ser Arg Asp Asn Ala Thr Leu Gln Ala Thr Leu His
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Ala Ala Arg Asp Thr Leu Ala Ser Val Phe Arg Leu Leu His Ser Leu
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Asp Gln Ala Lys Glu Glu Leu Glu Arg Leu Ala Ala Ser Leu Asp Gly
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Ala Arg Thr Pro Leu Leu Gln Arg Met Gln Thr Phe Ser Pro Ala Gly
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Ser Lys Leu Arg Leu Val Glu Ala Ala Glu Ala His Ala Gln Gln Leu
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2625 2630 2635 2640
Gln Asp Thr Ala Thr Arg Val Gln Ser Gln Leu Gln Ala Met Gln Glu
2645 2650 2655
Asn Val Glu Arg Trp Gln Gly Gln Tyr Glu Gly Leu Arg Gly Gln Asp
2660 2665 2670
Leu Gly Gln Ala Val Leu Asp Ala Gly His Ser Val Ser Thr Leu Glu
2675 2680 2685
Lys Thr Leu Pro Gln Leu Leu Ala Lys Leu Ser Ile Leu Glu Asn Arg
2690 2695 2700
Gly Val His Asn Ala Ser Leu Ala Leu Ser Ala Ser Ile Gly Arg Val
2705 2710 2715 2720
Arg Glu Leu Ile Ala Gln Ala Arg Gly Ala Ala Ser Lys Val Lys Val
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Pro Met Lys Phe Asn Gly Arg Ser Gly Val Gln Leu Arg Thr Pro Arg
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Asp Leu Ala Asp Leu Ala Ala Tyr Thr Ala Leu Lys Phe Tyr Leu Gln
2755 2760 2765
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2770 2775 2780
Tyr Met Gly Ser Arg Gln Ala Thr Gly Asp Tyr Met Gly Val Ser Leu
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Glu Gly Leu Leu Asn Leu Arg Pro Asp Asp Phe Val Phe Tyr Val Gly
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Gly Tyr Pro Ser Thr Phe Thr Pro Pro Pro Leu Leu Arg Phe Pro Gly
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Asp Leu Glu Leu Ala Asp Ala Tyr Tyr Leu Gly Gly Val Pro Pro Asp
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Gln Leu Pro Pro Ser Leu Arg Arg Leu Phe Pro Thr Gly Gly Ser Val
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Arg Gly Cys Val Lys Gly Ile Lys Ala Leu Gly Lys Tyr Val Asp Leu
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Lys Arg Leu Asn Thr Thr Gly Val Ser Ala Gly Cys Thr Ala Asp Leu
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Leu Val Gly Arg Ala Met Thr Phe His Gly His Gly Phe Leu Arg Leu
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Ala Leu Ser Asn Val Ala Pro Leu Thr Gly Asn Val Tyr Ser Gly Phe
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Gly Phe His Ser Ala Gln Asp Ser Ala Leu Leu Tyr Tyr Arg Ala Ser
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Pro Asp Gly Leu Cys Gln Val Ser Leu Gln Gln Gly Arg Val Ser Leu
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Gln Leu Leu Arg Thr Glu Val Lys Thr Gln Ala Gly Phe Ala Asp Gly
3185 3190 3195 3200
Ala Pro His Tyr Val Ala Phe Tyr Ser Asn Ala Thr Gly Val Trp Leu
3205 3210 3215
Tyr Val Asp Asp Gln Leu Gln Gln Met Lys Pro His Arg Gly Pro Pro
3220 3225 3230
Pro Glu Leu Gln Pro Gln Pro Glu Gly Pro Pro Arg Leu Leu Leu Gly
3235 3240 3245
Gly Leu Pro Glu Ser Gly Thr Ile Tyr Asn Phe Ser Gly Cys Ile Ser
3250 3255 3260
Asn Val Phe Val Gln Arg Leu Leu Gly Pro Gln Arg Val Phe Asp Leu
3265 3270 3275 3280

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Leu Gln Ala Gln Thr Pro Gly Leu Gly Pro Arg Gly Leu Gln Ala Thr
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Ala Arg Lys Ala Ser Arg Arg Ser Arg Gln Pro Ala Arg His Pro Ala
        3315                3320                3325
Cys Met Leu Pro Pro His Leu Arg Thr Thr Arg Asp Ser Tyr Gln Phe
    3330                3335                3340
Gly Gly Ser Leu Ser Ser His Leu Glu Phe Val Gly Ile Leu Ala Arg
3345                3350                3355                3360
His Arg Asn Trp Pro Ser Leu Ser Met His Val Leu Pro Arg Ser Ser
                3365                3370                3375
Arg Gly Leu Leu Leu Phe Thr Ala Arg Leu Arg Pro Gly Ser Pro Ser
            3380                3385                3390
Leu Ala Leu Phe Leu Ser Asn Gly His Phe Val Ala Gln Met Glu Gly
        3395                3400                3405
Leu Gly Thr Arg Leu Arg Ala Gln Ser Arg Gln Arg Ser Arg Pro Gly
    3410                3415                3420
Arg Trp His Lys Val Ser Val Arg Trp Glu Lys Asn Arg Ile Leu Leu
3425                3430                3435                3440
Val Thr Asp Gly Ala Arg Ala Trp Ser Gln Glu Gly Pro His Arg Gln
                3445                3450                3455
His Gln Gly Ala Glu His Pro Gln Pro His Thr Leu Phe Val Gly Gly
            3460                3465                3470
Leu Pro Ala Ser Ser His Ser Ser Lys Leu Pro Val Thr Val Gly Phe
        3475                3480                3485
Ser Gly Cys Val Lys Arg Leu Arg Leu His Gly Arg Pro Leu Gly Ala
    3490                3495                3500
Pro Thr Arg Met Ala Gly Val Thr Pro Cys Ile Leu Gly Pro Leu Glu
3505                3510                3515                3520
Ala Gly Leu Phe Phe Pro Gly Ser Gly Gly Val Ile Thr Leu Asp Leu
                3525                3530                3535
Pro Gly Ala Thr Leu Pro Asp Val Gly Leu Glu Leu Glu Val Arg Pro
            3540                3545                3550
Leu Ala Val Thr Gly Leu Ile Phe His Leu Gly Gln Ala Arg Thr Pro
        3555                3560                3565
Pro Tyr Leu Gln Leu Gln Val Thr Glu Lys Gln Val Leu Leu Arg Ala
    3570                3575                3580
Asp Asp Gly Ala Gly Glu Phe Ser Thr Ser Val Thr Arg Pro Ser Val
3585                3590                3595                3600
Leu Cys Asp Gly Gln Trp His Arg Leu Ala Val Met Lys Ser Gly Asn
                3605                3610                3615
Val Leu Arg Leu Glu Val Asp Ala Gln Ser Asn His Thr Val Gly Pro
            3620                3625                3630
Leu Leu Ala Ala Ala Ala Gly Ala Pro Ala Pro Leu Tyr Leu Gly Gly
        3635                3640                3645
Leu Pro Glu Pro Met Ala Val Gln Pro Trp Pro Pro Ala Tyr Cys Gly
    3650                3655                3660
Cys Met Arg Arg Leu Ala Val Asn Arg Ser Pro Val Ala Met Thr Arg
3665                3670                3675                3680
Ser Val Glu Val His Gly Ala Val Gly Ala Ser Gly Cys Pro Ala Ala
                3685                3690                3695
```

<210> 32
<211> 337
<212> PRT
<213> Homo sapiens

<400> 32
Met Thr Asn Asn Ser Gly Ser Lys Ala Glu Leu Val Val Gly Gly Lys
1 5 10 15
Tyr Lys Leu Val Arg Lys Ile Gly Ser Gly Ser Phe Gly Asp Val Tyr
20 25 30
Leu Gly Ile Thr Thr Thr Asn Gly Glu Asp Val Ala Val Lys Leu Glu
35 40 45
Ser Gln Lys Val Lys His Pro Gln Leu Leu Tyr Glu Ser Lys Leu Tyr
50 55 60
Thr Ile Leu Gln Gly Gly Val Gly Ile Pro His Met His Trp Tyr Gly
65 70 75 80
Gln Glu Lys Asp Asn Asn Val Leu Val Met Asp Leu Leu Gly Pro Ser
85 90 95
Leu Glu Asp Leu Phe Asn Phe Cys Ser Arg Arg Phe Thr Met Lys Thr
100 105 110
Val Leu Met Leu Ala Asp Gln Met Ile Ser Arg Ile Glu Tyr Val His
115 120 125
Thr Lys Asn Phe Leu His Arg Asp Ile Lys Pro Asp Asn Phe Leu Met
130 135 140
Gly Thr Gly Arg His Cys Asn Lys Leu Phe Leu Ile Asp Phe Gly Leu
145 150 155 160
Ala Lys Lys Tyr Arg Asp Asn Arg Thr Arg Gln His Ile Pro Tyr Arg
165 170 175
Glu Asp Lys His Leu Ile Gly Thr Val Arg Tyr Ala Ser Ile Asn Ala
180 185 190
His Leu Gly Ile Glu Gln Ser Arg Arg Asp Asp Met Glu Ser Leu Gly
195 200 205
Tyr Val Phe Met Tyr Phe Asn Arg Thr Ser Leu Pro Trp Gln Gly Leu
210 215 220
Arg Ala Met Thr Lys Lys Gln Lys Tyr Glu Lys Ile Ser Glu Lys Lys
225 230 235 240
Met Ser Thr Pro Val Glu Val Leu Cys Lys Gly Phe Pro Ala Glu Phe
245 250 255
Ala Met Tyr Leu Asn Tyr Cys Arg Gly Leu Arg Phe Glu Glu Val Pro
260 265 270
Asp Tyr Met Tyr Leu Arg Gln Leu Phe Arg Ile Leu Phe Arg Thr Leu
275 280 285
Asn His Gln Tyr Asp Tyr Thr Phe Asp Trp Thr Met Leu Lys Gln Lys
290 295 300
Ala Ala Gln Gln Ala Ala Ser Ser Ser Gly Gln Gly Gln Gln Ala Gln
305 310 315 320
Thr Gln Thr Gly Lys Gln Thr Glu Lys Asn Lys Asn Asn Val Lys Asp
325 330 335
Asn

<210> 33
<211> 888
<212> PRT
<213> Homo sapiens

<400> 33
Met Glu Ser Leu Leu Leu Pro Val Leu Leu Leu Leu Ala Ile Leu Trp
1 5 10 15
Thr Gln Ala Ala Ala Leu Ile Asn Leu Lys Tyr Ser Val Glu Glu Glu
20 25 30
Gln Arg Ala Gly Thr Val Ile Ala Asn Val Ala Lys Asp Ala Arg Glu
35 40 45

```
Ala Gly Phe Ala Leu Asp Pro Arg Gln Ala Ser Ala Phe Arg Val Val
    50                  55                  60
Ser Asn Ser Ala Pro His Leu Val Asp Ile Asn Pro Ser Ser Gly Leu
65                  70                  75                  80
Leu Val Thr Lys Gln Lys Ile Asp Arg Asp Leu Leu Cys Arg Gln Ser
                85                  90                  95
Pro Lys Cys Ile Ile Ser Leu Glu Val Met Ser Ser Ser Met Glu Ile
            100                 105                 110
Cys Val Ile Lys Val Glu Ile Lys Asp Leu Asn Asp Asn Ala Pro Ser
        115                 120                 125
Phe Pro Ala Ala Gln Ile Glu Leu Glu Ile Ser Glu Ala Ala Ser Pro
    130                 135                 140
Gly Thr Arg Ile Pro Leu Asp Ser Ala Tyr Asp Pro Asp Ser Gly Ser
145                 150                 155                 160
Phe Gly Val Gln Thr Tyr Glu Leu Thr Pro Asn Glu Leu Phe Gly Leu
                165                 170                 175
Glu Ile Lys Thr Arg Gly Asp Gly Ser Arg Phe Ala Glu Leu Val Val
            180                 185                 190
Glu Lys Ser Leu Asp Arg Glu Thr Gln Ser His Tyr Ser Phe Arg Ile
        195                 200                 205
Thr Ala Leu Asp Gly Gly Asp Pro Pro Arg Leu Gly Thr Val Gly Leu
    210                 215                 220
Ser Ile Lys Val Thr Asp Ser Asn Asp Asn Asn Pro Val Phe Ser Glu
225                 230                 235                 240
Ser Thr Tyr Ala Val Ser Val Pro Glu Asn Ser Pro Pro Asn Thr Pro
                245                 250                 255
Val Ile Arg Leu Asn Ala Ser Asp Pro Asp Glu Gly Thr Asn Gly Gln
            260                 265                 270
Val Val Tyr Ser Phe Tyr Gly Tyr Val Asn Asp Arg Thr Arg Glu Leu
        275                 280                 285
Phe Gln Ile Asp Pro His Ser Gly Leu Val Thr Val Thr Gly Ala Leu
    290                 295                 300
Asp Tyr Glu Glu Gly His Val Tyr Glu Leu Asp Val Gln Ala Lys Asp
305                 310                 315                 320
Leu Gly Pro Asn Ser Ile Pro Ala His Cys Lys Val Thr Val Ser Val
                325                 330                 335
Leu Asp Thr Asn Asp Asn Pro Pro Val Ile Asn Leu Leu Ser Val Asn
            340                 345                 350
Ser Glu Leu Val Glu Val Ser Glu Ser Ala Pro Pro Gly Tyr Val Ile
        355                 360                 365
Ala Leu Val Arg Val Ser Asp Arg Asp Ser Gly Leu Asn Gly Arg Val
    370                 375                 380
Gln Cys Arg Leu Leu Gly Asn Val Pro Phe Arg Leu Gln Glu Tyr Glu
385                 390                 395                 400
Ser Phe Ser Thr Ile Leu Val Asp Gly Arg Leu Asp Arg Glu Gln His
                405                 410                 415
Asp Gln Tyr Asn Leu Thr Ile Gln Ala Arg Asp Gly Gly Val Pro Met
            420                 425                 430
Leu Gln Ser Ala Lys Ser Phe Thr Val Leu Ile Thr Asp Glu Asn Asp
        435                 440                 445
Asn His Pro His Phe Ser Lys Pro Tyr Tyr Gln Val Ile Val Gln Glu
    450                 455                 460
Asn Asn Thr Pro Gly Ala Tyr Leu Leu Ser Val Ser Ala Arg Asp Pro
465                 470                 475                 480
Asp Leu Gly Leu Asn Gly Ser Val Ser Tyr Gln Ile Val Pro Ser Gln
                485                 490                 495
Val Arg Asp Met Pro Val Phe Thr Tyr Val Ser Ile Asn Pro Asn Ser
            500                 505                 510
Gly Asp Ile Tyr Ala Leu Arg Ser Phe Asn His Glu Gln Thr Lys Ala
```

```
        515                 520                 525
Phe Glu Phe Lys Val Leu Ala Lys Asp Gly Gly Leu Pro Ser Leu Gln
    530                 535                 540
Ser Asn Ala Thr Val Arg Val Ile Ile Leu Asp Val Asn Asp Asn Thr
545                 550                 555                 560
Pro Val Ile Thr Ala Pro Pro Leu Ile Asn Gly Thr Ala Glu Val Tyr
                565                 570                 575
Ile Pro Arg Asn Ser Gly Ile Gly Tyr Leu Val Thr Val Val Lys Ala
            580                 585                 590
Glu Asp Tyr Asp Glu Gly Glu Asn Gly Arg Val Thr Tyr Asp Met Thr
        595                 600                 605
Glu Gly Asp Arg Gly Phe Phe Glu Ile Asp Gln Val Asn Gly Glu Val
    610                 615                 620
Arg Thr Thr Arg Thr Phe Gly Glu Ser Ser Lys Ser Ser Tyr Glu Leu
625                 630                 635                 640
Ile Val Val Ala His Asp His Gly Lys Thr Ser Leu Ser Ala Ser Ala
                645                 650                 655
Leu Val Leu Ile Tyr Leu Ser Pro Ala Leu Asp Ala Gln Glu Ser Met
            660                 665                 670
Gly Ser Val Asn Leu Ser Leu Ile Phe Ile Ile Ala Leu Gly Ser Ile
        675                 680                 685
Ala Gly Ile Leu Phe Val Thr Met Ile Phe Val Ala Ile Lys Cys Lys
    690                 695                 700
Arg Asp Asn Lys Glu Ile Arg Thr Tyr Asn Cys Ser Asn Cys Leu Thr
705                 710                 715                 720
Ile Thr Cys Leu Leu Gly Cys Phe Ile Lys Gly Gln Asn Ser Lys Cys
                725                 730                 735
Leu His Cys Ile Ser Val Ser Pro Ile Ser Glu Glu Gln Asp Lys Lys
            740                 745                 750
Thr Glu Glu Lys Val Ser Leu Arg Gly Lys Arg Ile Ala Glu Tyr Ser
        755                 760                 765
Tyr Gly His Gln Lys Lys Ser Ser Lys Lys Lys Lys Ile Ser Lys Asn
    770                 775                 780
Asp Ile Arg Leu Val Pro Arg Asp Val Glu Glu Thr Asp Lys Met Asn
785                 790                 795                 800
Val Val Ser Cys Ser Ser Leu Thr Ser Ser Leu Asn Tyr Phe Asp Tyr
                805                 810                 815
His Gln Gln Thr Leu Pro Leu Gly Cys Arg Arg Ser Glu Ser Thr Phe
            820                 825                 830
Leu Asn Val Glu Asn Gln Asn Thr Arg Asn Thr Ser Ala Asn His Ile
        835                 840                 845
Tyr His His Ser Phe Asn Ser Gln Gly Pro Gln Gln Pro Asp Leu Ile
    850                 855                 860
Ile Asn Gly Val Pro Leu Pro Glu Val Ser Ala Ala Lys Trp Leu Cys
865                 870                 875                 880
Glu Val Leu Pro Gly Leu Leu Leu
                885
```

<210> 34
<211> 855
<212> PRT
<213> Homo sapiens

<400> 34

```
Met Glu Ser Leu Leu Leu Pro Val Leu Leu Leu Leu Ala Ile Leu Trp
 1               5                  10                  15
Thr Gln Ala Ala Ala Leu Ile Asn Leu Lys Tyr Ser Val Glu Glu Glu
            20                  25                  30
```

```
Gln Arg Ala Gly Thr Val Ile Ala Asn Val Ala Lys Asp Ala Arg Glu
        35                  40                  45
Ala Gly Phe Ala Leu Asp Pro Arg Gln Ala Ser Ala Phe Arg Val Val
    50                  55                  60
Ser Asn Ser Ala Pro His Leu Val Asp Ile Asn Pro Ser Ser Gly Leu
65                  70                  75                  80
Leu Val Thr Lys Gln Lys Ile Asp Arg Asp Leu Leu Cys Arg Gln Ser
                85                  90                  95
Pro Lys Cys Ile Ile Ser Leu Glu Val Met Ser Ser Ser Met Glu Ile
            100                 105                 110
Cys Val Ile Lys Val Glu Ile Lys Asp Leu Asn Asp Asn Ala Pro Ser
        115                 120                 125
Phe Pro Ala Ala Gln Ile Glu Leu Glu Ile Ser Glu Ala Ala Ser Pro
    130                 135                 140
Gly Thr Arg Ile Pro Leu Asp Ser Ala Tyr Asp Pro Asp Ser Gly Ser
145                 150                 155                 160
Phe Gly Val Gln Thr Tyr Glu Leu Thr Pro Asn Glu Leu Phe Gly Leu
                165                 170                 175
Glu Ile Lys Thr Arg Gly Asp Gly Ser Arg Phe Ala Glu Leu Val Val
            180                 185                 190
Glu Lys Ser Leu Asp Arg Glu Thr Gln Ser His Tyr Ser Phe Arg Ile
        195                 200                 205
Thr Ala Leu Asp Gly Gly Asp Pro Pro Arg Leu Gly Thr Val Gly Leu
    210                 215                 220
Ser Ile Lys Val Thr Asp Ser Asn Asp Asn Asn Pro Val Phe Ser Glu
225                 230                 235                 240
Ser Thr Tyr Ala Val Ser Val Pro Glu Asn Ser Pro Pro Asn Thr Pro
                245                 250                 255
Val Ile Arg Leu Asn Ala Ser Asp Pro Asp Glu Gly Thr Asn Gly Gln
            260                 265                 270
Val Val Tyr Ser Phe Tyr Gly Tyr Val Asn Asp Arg Thr Arg Glu Leu
        275                 280                 285
Phe Gln Ile Asp Pro His Ser Gly Leu Val Thr Val Thr Gly Ala Leu
    290                 295                 300
Asp Tyr Glu Glu Gly His Val Tyr Glu Leu Asp Val Gln Ala Lys Asp
305                 310                 315                 320
Leu Gly Pro Asn Ser Ile Pro Ala His Cys Lys Val Thr Val Ser Val
                325                 330                 335
Leu Asp Thr Asn Asp Asn Pro Pro Val Ile Asn Leu Leu Ser Val Asn
            340                 345                 350
Ser Glu Leu Val Glu Val Ser Glu Ser Ala Pro Pro Gly Tyr Val Ile
        355                 360                 365
Ala Leu Val Arg Val Ser Asp Arg Asp Ser Gly Leu Asn Gly Arg Val
    370                 375                 380
Gln Cys Arg Leu Leu Gly Asn Val Pro Phe Arg Leu Gln Glu Tyr Glu
385                 390                 395                 400
Ser Phe Ser Thr Ile Leu Val Asp Gly Arg Leu Asp Arg Glu Gln His
                405                 410                 415
Asp Gln Tyr Asn Leu Thr Ile Gln Ala Arg Asp Gly Gly Val Pro Met
            420                 425                 430
Leu Gln Ser Ala Lys Ser Phe Thr Val Leu Ile Thr Asp Glu Asn Asp
        435                 440                 445
Asn His Pro His Phe Ser Lys Pro Tyr Tyr Gln Val Ile Val Gln Glu
    450                 455                 460
Asn Asn Thr Pro Gly Ala Tyr Leu Leu Ser Val Ser Ala Arg Asp Pro
465                 470                 475                 480
Asp Leu Gly Leu Asn Gly Ser Val Ser Tyr Gln Ile Val Pro Ser Gln
                485                 490                 495
Val Arg Asp Met Pro Val Phe Thr Tyr Val Ser Ile Asn Pro Asn Ser
```

```
            500                 505                 510
Gly Asp Ile Tyr Ala Leu Arg Ser Phe Asn His Glu Gln Thr Lys Ala
        515                 520                 525
Phe Glu Phe Lys Val Leu Ala Lys Asp Gly Gly Leu Pro Ser Leu Gln
    530                 535                 540
Ser Asn Ala Thr Val Arg Val Ile Ile Leu Asp Val Asn Asp Asn Thr
545                 550                 555                 560
Pro Val Ile Thr Ala Pro Pro Leu Ile Asn Gly Thr Ala Glu Val Tyr
                565                 570                 575
Ile Pro Arg Asn Ser Gly Ile Gly Tyr Leu Val Thr Val Val Lys Ala
            580                 585                 590
Glu Asp Tyr Asp Glu Gly Glu Asn Gly Arg Val Thr Tyr Asp Met Thr
        595                 600                 605
Glu Gly Asp Arg Gly Phe Phe Glu Ile Asp Gln Val Asn Gly Glu Val
    610                 615                 620
Arg Thr Thr Arg Thr Phe Gly Glu Ser Ser Lys Ser Ser Tyr Glu Leu
625                 630                 635                 640
Ile Val Val Ala His Asp His Gly Lys Thr Ser Leu Ser Ala Ser Ala
                645                 650                 655
Leu Val Leu Ile Tyr Leu Ser Pro Ala Leu Asp Ala Gln Glu Ser Met
            660                 665                 670
Gly Ser Val Asn Leu Ser Leu Ile Phe Ile Ile Ala Leu Gly Ser Ile
        675                 680                 685
Ala Gly Ile Leu Phe Val Thr Met Ile Phe Val Ala Ile Lys Cys Lys
    690                 695                 700
Arg Asp Asn Lys Glu Ile Arg Thr Tyr Asn Cys Arg Ile Ala Glu Tyr
705                 710                 715                 720
Ser Tyr Gly His Gln Lys Lys Ser Ser Lys Lys Lys Lys Ile Ser Lys
                725                 730                 735
Asn Asp Ile Arg Leu Val Pro Arg Asp Val Glu Glu Thr Asp Lys Met
            740                 745                 750
Asn Val Val Ser Cys Ser Ser Leu Thr Ser Ser Leu Asn Tyr Phe Asp
        755                 760                 765
Tyr His Gln Gln Thr Leu Pro Leu Gly Cys Arg Arg Ser Glu Ser Thr
    770                 775                 780
Phe Leu Asn Val Glu Asn Gln Asn Thr Arg Asn Thr Ser Ala Asn His
785                 790                 795                 800
Ile Tyr His His Ser Phe Asn Ser Gln Gly Pro Gln Gln Pro Asp Leu
                805                 810                 815
Ile Ile Asn Gly Val Pro Leu Pro Glu Thr Glu Asn Tyr Ser Phe Asp
            820                 825                 830
Ser Asn Tyr Val Asn Ser Arg Ala His Leu Ile Lys Arg Tyr Val Gly
        835                 840                 845
Leu Leu Ala Tyr Cys Cys Asn
    850                 855
```

<210> 35
<211> 329
<212> PRT
<213> Homo sapiens

<400> 35

```
Met Val Thr Lys Ala Phe Val Leu Leu Ala Ile Phe Ala Glu Ala Ser
 1                5                  10                  15
Ala Lys Ser Cys Ala Pro Asn Lys Ala Asp Val Ile Leu Val Phe Cys
            20                  25                  30
Tyr Pro Lys Thr Ile Ile Thr Lys Ile Pro Glu Cys Pro Tyr Gly Trp
        35                  40                  45
```

```
Glu Val His Gln Leu Ala Leu Gly Gly Leu Cys Tyr Asn Gly Val His
 50                  55                  60
Glu Gly Gly Tyr Tyr Gln Phe Val Ile Pro Asp Leu Ser Pro Lys Asn
65                  70                  75                  80
Lys Ser Tyr Cys Gly Thr Gln Ser Glu Tyr Lys Pro Pro Ile Tyr His
                85                  90                  95
Phe Tyr Ser His Ile Val Ser Asn Asp Thr Thr Val Ile Val Lys Asn
            100                 105                 110
Gln Pro Val Asn Tyr Ser Phe Ser Cys Thr Tyr His Ser Thr Tyr Leu
        115                 120                 125
Val Asn Gln Ala Ala Phe Asp Gln Arg Val Ala Thr Val His Val Lys
    130                 135                 140
Asn Gly Ser Met Gly Thr Phe Glu Ser Gln Leu Ser Leu Asn Phe Tyr
145                 150                 155                 160
Thr Asn Ala Lys Phe Ser Ile Lys Lys Glu Ala Pro Phe Val Leu Glu
                165                 170                 175
Ala Ser Glu Ile Gly Ser Asp Leu Phe Ala Gly Val Glu Ala Lys Gly
            180                 185                 190
Leu Ser Ile Arg Phe Lys Val Val Leu Asn Ser Cys Trp Ala Thr Pro
        195                 200                 205
Ser Ala Asp Phe Met Tyr Pro Leu Gln Trp Gln Leu Ile Asn Lys Gly
    210                 215                 220
Cys Pro Thr Asp Glu Thr Val Leu Val His Glu Asn Gly Arg Asp His
225                 230                 235                 240
Arg Ala Thr Phe Gln Phe Asn Ala Phe Arg Phe Gln Asn Ile Pro Lys
                245                 250                 255
Leu Ser Lys Val Trp Leu His Cys Glu Thr Phe Ile Cys Asp Ser Glu
            260                 265                 270
Lys Leu Ser Cys Pro Val Thr Cys Asp Lys Arg Lys Arg Leu Leu Arg
        275                 280                 285
Asp Gln Thr Gly Gly Val Leu Val Val Glu Leu Ser Leu Arg Ser Arg
    290                 295                 300
Gly Phe Ser Ser Leu Tyr Ser Phe Ser Asp Val Leu His His Leu Ile
305                 310                 315                 320
Met Met Leu Gly Ile Cys Ala Val Leu
                325
```

<210> 36
<211> 232
<212> PRT
<213> Homo sapiens

<400> 36

```
Met Leu Tyr Thr Arg Lys Asn Leu Thr Cys Ala Gln Thr Ile Asn Ser
 1               5                  10                  15
Ser Ala Phe Gly Asn Leu Asn Val Thr Lys Lys Thr Thr Phe Ile Val
            20                  25                  30
His Gly Phe Arg Pro Thr Gly Ser Pro Pro Val Trp Met Asp Asp Leu
        35                  40                  45
Val Lys Gly Leu Leu Ser Val Glu Asp Met Asn Val Val Val Val Asp
    50                  55                  60
Trp Asn Arg Gly Ala Thr Thr Leu Ile Tyr Thr His Ala Ser Ser Lys
65                  70                  75                  80
Thr Arg Lys Val Ala Met Val Leu Lys Glu Phe Ile Asp Gln Met Leu
                85                  90                  95
Ala Glu Gly Ala Ser Leu Asp Asp Ile Tyr Met Ile Gly Val Ser Leu
            100                 105                 110
Gly Ala His Ile Ser Gly Phe Val Gly Glu Met Tyr Asp Gly Trp Leu
```

```
        115                 120                 125
Gly Arg Ile Thr Gly Leu Asp Pro Ala Gly Pro Leu Phe Asn Gly Lys
    130                 135                 140
Pro His Gln Asp Arg Leu Asp Pro Ser Asp Ala Gln Phe Val Asp Val
145                 150                 155                 160
Ile His Ser Asp Thr Asp Gly Asn Ala Pro Phe Leu Val Ala Leu Gly
                165                 170                 175
Tyr Lys Glu Pro Leu Gly Asn Ile Asp Phe Tyr Pro Asn Gly Gly Leu
            180                 185                 190
Asp Gln Pro Gly Cys Pro Lys Thr Ile Leu Gly Gly Asn Val Lys Glu
        195                 200                 205
Met Ile Gln Ala Ser Tyr Ile Phe Phe Leu Lys Asn Asp Ser Met Asp
    210                 215                 220
Leu Ser Ser Pro Lys Glu Val Glu
225                 230
```

<210> 37
<211> 452
<212> PRT
<213> Homo sapiens

<400> 37

```
Met Leu Arg Phe Tyr Leu Phe Ile Ser Leu Leu Cys Leu Ser Arg Ser
 1               5                  10                  15
Asp Ala Glu Glu Thr Cys Pro Ser Phe Thr Arg Leu Ser Phe His Ser
            20                  25                  30
Ala Val Val Gly Thr Gly Leu Asn Val Arg Leu Met Leu Tyr Thr Arg
        35                  40                  45
Lys Asn Leu Thr Cys Ala Gln Thr Ile Asn Ser Ser Ala Phe Gly Asn
    50                  55                  60
Leu Asn Val Thr Lys Lys Thr Thr Phe Ile Val His Gly Phe Arg Pro
65                  70                  75                  80
Thr Gly Ser Pro Pro Val Trp Met Asp Asp Leu Val Lys Gly Leu Leu
                85                  90                  95
Ser Val Glu Asp Met Asn Val Val Val Val Asp Trp Asn Arg Gly Ala
            100                 105                 110
Thr Thr Leu Ile Tyr Thr His Ala Ser Ser Lys Thr Arg Lys Val Ala
        115                 120                 125
Met Val Leu Lys Glu Phe Ile Asp Gln Met Leu Ala Glu Gly Ala Ser
    130                 135                 140
Leu Asp Asp Ile Tyr Met Ile Gly Val Ser Leu Gly Ala His Ile Ser
145                 150                 155                 160
Gly Phe Val Gly Glu Met Tyr Asp Gly Trp Leu Gly Arg Ile Thr Gly
                165                 170                 175
Leu Asp Pro Ala Gly Pro Leu Phe Asn Gly Lys Pro His Gln Asp Arg
            180                 185                 190
Leu Asp Pro Ser Asp Ala Gln Phe Val Asp Val Ile His Ser Asp Thr
        195                 200                 205
Asp Ala Leu Gly Tyr Lys Glu Pro Leu Gly Asn Ile Asp Phe Tyr Pro
    210                 215                 220
Asn Gly Gly Leu Asp Gln Pro Gly Cys Pro Lys Thr Ile Leu Gly Gly
225                 230                 235                 240
Phe Gln Tyr Phe Lys Cys Asp His Gln Arg Ser Val Tyr Leu Tyr Leu
                245                 250                 255
Ser Ser Leu Arg Glu Ser Cys Thr Ile Thr Ala Tyr Pro Cys Asp Ser
            260                 265                 270
Tyr Gln Asp Tyr Arg Asn Gly Lys Cys Val Ser Cys Gly Thr Ser Gln
        275                 280                 285
```

```
Lys Glu Ser Cys Pro Leu Leu Gly Tyr Tyr Ala Asp Asn Trp Lys Asp
    290                 295                 300
His Leu Arg Gly Lys Asp Pro Pro Met Thr Lys Ala Phe Phe Asp Thr
305                 310                 315                 320
Ala Glu Glu Ser Pro Phe Cys Met Tyr His Tyr Phe Val Asp Ile Ile
                325                 330                 335
Thr Trp Asp Lys Asn Val Arg Arg Gly Asp Ile Thr Ile Lys Leu Arg
            340                 345                 350
Asp Lys Ala Gly Asn Thr His Arg Ser Lys Ile Ile Ser Asn Glu Pro
        355                 360                 365
Thr Thr Phe Gln Lys Tyr His Gln Val Ser Leu Leu Ala Arg Phe Asn
    370                 375                 380
Gln Asp Leu Asp Lys Val Ala Ala Ile Ser Leu Met Phe Ser Thr Gly
385                 390                 395                 400
Ser Leu Ile Gly Pro Arg Tyr Lys Leu Arg Ile Leu Arg Met Lys Leu
                405                 410                 415
Arg Ser Leu Ala His Pro Glu Arg Pro Gln Leu Cys Arg Tyr Asp Leu
            420                 425                 430
Val Leu Met Glu Asn Val Glu Thr Val Phe Gln Pro Ile Leu Cys Pro
        435                 440                 445
Glu Leu Gln Leu
    450
```

<210> 38
<211> 450
<212> PRT
<213> Homo sapiens

<400> 38

```
Met Gly Leu Arg Ser His His Leu Ser Leu Gly Leu Leu Leu Leu Phe
 1                   5                  10                  15
Leu Leu Pro Ala Glu Cys Leu Gly Ala Glu Gly Arg Leu Ala Leu Lys
            20                  25                  30
Leu Phe Arg Asp Leu Phe Ala Asn Tyr Thr Ser Ala Leu Arg Pro Val
        35                  40                  45
Ala Asp Thr Asp Gln Thr Leu Asn Val Thr Leu Glu Val Thr Leu Ser
    50                  55                  60
Gln Ile Ile Asp Met Asp Glu Arg Asn Gln Val Leu Thr Leu Tyr Leu
65                  70                  75                  80
Trp Ile Arg Gln Glu Trp Thr Asp Ala Tyr Leu Arg Trp Asp Pro Asn
                85                  90                  95
Ala Tyr Gly Gly Leu Asp Ala Ile Arg Ile Pro Ser Ser Leu Val Trp
            100                 105                 110
Arg Pro Asp Ile Val Leu Tyr Asn Lys Ala Asp Ala Gln Pro Pro Gly
        115                 120                 125
Ser Ala Ser Thr Asn Val Val Leu Arg His Asp Gly Ala Val Arg Trp
    130                 135                 140
Asp Ala Pro Ala Ile Thr Arg Ser Ser Cys Arg Val Asp Val Ala Ala
145                 150                 155                 160
Phe Pro Phe Asp Ala Gln His Cys Gly Leu Thr Phe Gly Ser Trp Thr
                165                 170                 175
His Gly Gly His Gln Leu Asp Val Arg Pro Arg Gly Ala Ala Ala Ser
            180                 185                 190
Leu Ala Asp Phe Val Glu Asn Val Glu Trp Arg Val Leu Gly Met Pro
        195                 200                 205
Ala Arg Arg Arg Val Leu Thr Tyr Gly Cys Cys Ser Glu Pro Tyr Pro
    210                 215                 220
Asp Val Thr Phe Thr Leu Leu Leu Arg Arg Arg Ala Ala Ala Tyr Val
```

225 230 235 240
Cys Asn Leu Leu Leu Pro Cys Val Leu Ile Ser Leu Leu Ala Pro Leu
245 250 255
Ala Phe His Leu Pro Ala Asp Ser Gly Glu Lys Val Ser Leu Gly Val
260 265 270
Thr Val Leu Leu Ala Leu Thr Val Phe Gln Leu Leu Leu Ala Glu Ser
275 280 285
Met Pro Pro Ala Glu Ser Val Pro Leu Ile Gly Lys Tyr Tyr Met Ala
290 295 300
Thr Met Thr Met Val Thr Phe Ser Thr Ala Leu Thr Ile Leu Ile Met
305 310 315 320
Asn Leu His Tyr Cys Gly Pro Ser Val Arg Pro Val Pro Ala Trp Ala
325 330 335
Arg Ala Leu Leu Leu Gly His Leu Ala Arg Gly Leu Cys Val Arg Glu
340 345 350
Arg Gly Glu Pro Cys Gly Gln Ser Arg Pro Pro Glu Leu Ser Pro Ser
355 360 365
Pro Gln Ser Pro Glu Gly Gly Ala Gly Pro Pro Ala Gly Pro Cys His
370 375 380
Glu Pro Arg Cys Leu Cys Arg Gln Glu Ala Leu Leu His His Val Ala
385 390 395 400
Thr Ile Ala Asn Thr Phe Arg Ser His Arg Ala Ala Gln Arg Cys His
405 410 415
Glu Asp Trp Lys Arg Leu Ala Arg Val Met Asp Arg Phe Phe Leu Ala
420 425 430
Ile Phe Phe Ser Met Ala Leu Val Met Ser Leu Leu Val Leu Val Gln
435 440 445
Ala Leu
450

<210> 39
<211> 255
<212> PRT
<213> Homo sapiens

<400> 39
Met Val Lys Gly Glu Lys Gly Pro Lys Gly Lys Lys Ile Thr Leu Lys
1 5 10 15
Val Ala Arg Asn Cys Ile Lys Ile Thr Phe Asp Gly Lys Lys Arg Leu
20 25 30
Asp Leu Ser Lys Met Gly Ile Thr Thr Phe Pro Lys Cys Ile Leu Arg
35 40 45
Leu Ser Asp Met Asp Glu Leu Asp Leu Ser Arg Asn Leu Ile Arg Lys
50 55 60
Ile Pro Asp Ser Ile Ser Lys Phe Gln Asn Leu Arg Trp Leu Asp Leu
65 70 75 80
His Ser Asn Tyr Ile Asp Lys Leu Pro Glu Ser Ile Gly Gln Met Thr
85 90 95
Ser Leu Leu Tyr Leu Asn Val Ser Asn Asn Arg Leu Thr Ser Asn Gly
100 105 110
Leu Pro Val Glu Leu Lys Gln Leu Lys Asn Ile Arg Ala Val Asn Leu
115 120 125
Gly Leu Asn His Leu Asp Ser Val Pro Thr Thr Leu Gly Ala Leu Lys
130 135 140
Glu Leu His Glu Val Gly Leu His Asp Asn Leu Leu Asn Asn Ile Pro
145 150 155 160
Val Ser Ile Ser Lys Leu Pro Lys Leu Lys Lys Leu Asn Ile Lys Arg
165 170 175

```
Asn Pro Phe Pro Lys Pro Gly Glu Ser Glu Ile Phe Ile Asp Ser Ile
            180                 185                 190
Arg Arg Leu Glu Asn Leu Tyr Val Val Glu Glu Lys Asp Leu Cys Ala
        195                 200                 205
Ala Cys Leu Arg Lys Cys Gln Asn Ala Arg Asp Asn Leu Asn Arg Ile
    210                 215                 220
Lys Asn Met Ala Thr Thr Thr Pro Arg Lys Thr Ile Phe Pro Asn Leu
225                 230                 235                 240
Ile Ser Pro Asn Ser Met Ala Lys Asp Ser Trp Glu Asp Trp Arg
                245                 250                 255
```

<210> 40
<211> 214
<212> PRT
<213> Homo sapiens

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<400> 40
Met Gln Ala Gly Thr Gln Ser Thr His Glu Ser Leu Lys Pro Gln Arg
 1               5                  10                  15
Val Gln Phe Gln Ser Arg Asn Phe His Asn Ile Leu Gln Trp Gln Pro
            20                  25                  30
Gly Arg Ala Leu Thr Gly Asn Ser Ser Val Tyr Phe Val Gln Tyr Lys
        35                  40                  45
Ile Tyr Gly Gln Arg Gln Trp Lys Asn Lys Glu Asp Cys Trp Gly Thr
    50                  55                  60
Gln Glu Leu Ser Cys Asp Leu Thr Ser Glu Thr Ser Asp Ile Gln Glu
65                  70                  75                  80
Pro Tyr Tyr Gly Arg Val Arg Ala Ala Ser Ala Gly Ser Tyr Ser Glu
                85                  90                  95
Trp Ser Met Thr Pro Arg Phe Thr Pro Trp Trp Glu Thr Lys Ile Asp
            100                 105                 110
Pro Pro Val Met Asn Ile Thr Gln Val Asn Gly Ser Leu Leu Val Ile
        115                 120                 125
Leu His Ala Pro Asn Leu Pro Tyr Arg Tyr Gln Lys Glu Lys Asn Val
    130                 135                 140
Ser Ile Glu Asp Tyr Tyr Glu Leu Leu Tyr Arg Val Phe Ile Ile Asn
145                 150                 155                 160
Asn Ser Leu Glu Lys Glu Gln Lys Val Tyr Glu Gly Ala His Arg Ala
                165                 170                 175
Val Glu Ile Glu Ala Leu Thr Pro His Ser Ser Tyr Cys Val Val Ala
            180                 185                 190
Glu Ile Tyr Gln Pro Met Leu Asp Arg Arg Ser Gln Arg Ser Glu Glu
        195                 200                 205
Arg Cys Val Glu Ile Pro
    210
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<210> 41
<211> 231
<212> PRT
<213> Homo sapiens

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<400> 41
Met Met Pro Lys His Cys Phe Leu Gly Phe Leu Ile Ser Phe Phe Leu
 1               5                  10                  15
Thr Gly Val Ala Gly Thr Gln Ser Thr His Glu Ser Leu Lys Pro Gln
            20                  25                  30
Arg Val Gln Phe Gln Ser Arg Asn Phe His Asn Ile Leu Gln Trp Gln
```

```
        35                  40                  45
Pro Gly Arg Ala Leu Thr Gly Asn Ser Ser Val Tyr Phe Val Gln Tyr
    50                  55                  60
Lys Ile Tyr Gly Gln Arg Gln Trp Lys Asn Lys Glu Asp Cys Trp Gly
65                  70                  75                  80
Thr Gln Glu Leu Ser Cys Asp Leu Thr Ser Glu Thr Ser Asp Ile Gln
                85                  90                  95
Glu Pro Tyr Tyr Gly Arg Val Arg Ala Ala Ser Ala Gly Ser Tyr Ser
            100                 105                 110
Glu Trp Ser Met Thr Pro Arg Phe Thr Pro Trp Trp Glu Thr Lys Ile
        115                 120                 125
Asp Pro Pro Val Met Asn Ile Thr Gln Val Asn Gly Ser Leu Leu Val
    130                 135                 140
Ile Leu His Ala Pro Asn Leu Pro Tyr Arg Tyr Gln Lys Glu Lys Asn
145                 150                 155                 160
Val Ser Ile Glu Asp Tyr Tyr Glu Leu Leu Tyr Arg Val Phe Ile Ile
                165                 170                 175
Asn Asn Ser Leu Glu Lys Glu Gln Lys Val Tyr Glu Gly Ala His Arg
            180                 185                 190
Ala Val Glu Ile Glu Ala Leu Thr Pro His Ser Ser Tyr Cys Val Val
        195                 200                 205
Ala Glu Ilé Tyr Gln Pro Met Leu Asp Arg Arg Ser Gln Arg Ser Glu
    210                 215                 220
Glu Arg Cys Val Glu Ile Pro
225                 230
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<210> 42
<211> 263
<212> PRT
<213> Homo sapiens

<400> 42

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Met Met Pro Lys His Cys Phe Leu Gly Phe Leu Ile Ser Phe Phe Leu
 1               5                  10                  15
Thr Gly Val Ala Gly Thr Gln Ser Thr His Glu Ser Leu Lys Pro Gln
            20                  25                  30
Arg Val Gln Phe Gln Ser Arg Asn Phe His Asn Ile Leu Gln Trp Gln
        35                  40                  45
Pro Gly Arg Ala Leu Thr Gly Asn Ser Ser Val Tyr Phe Val Gln Tyr
    50                  55                  60
Lys Ile Met Phe Ser Cys Ser Met Lys Ser Ser His Gln Lys Pro Ser
65                  70                  75                  80
Gly Cys Trp Gln His Ile Ser Cys Asn Phe Pro Gly Cys Arg Thr Leu
                85                  90                  95
Ala Lys Tyr Gly Gln Arg Gln Trp Lys Asn Lys Glu Asp Cys Trp Gly
            100                 105                 110
Thr Gln Glu Leu Ser Cys Asp Leu Thr Ser Glu Thr Ser Asp Ile Gln
        115                 120                 125
Glu Pro Tyr Tyr Gly Arg Val Arg Ala Ala Ser Ala Gly Ser Tyr Ser
    130                 135                 140
Glu Trp Ser Met Thr Pro Arg Phe Thr Pro Trp Trp Glu Thr Lys Ile
145                 150                 155                 160
Asp Pro Pro Val Met Asn Ile Thr Gln Val Asn Gly Ser Leu Leu Val
                165                 170                 175
Ile Leu His Ala Pro Asn Leu Pro Tyr Arg Tyr Gln Lys Glu Lys Asn
            180                 185                 190
Val Ser Ile Glu Asp Tyr Tyr Glu Leu Leu Tyr Arg Val Phe Ile Ile
        195                 200                 205
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Asn Asn Ser Leu Glu Lys Glu Gln Lys Val Tyr Glu Gly Ala His Arg
    210                 215                 220
Ala Val Glu Ile Glu Ala Leu Thr Pro His Ser Ser Tyr Cys Val Val
225                 230                 235                 240
Ala Glu Ile Tyr Gln Pro Met Leu Asp Arg Arg Ser Gln Arg Ser Glu
                245                 250                 255
Glu Arg Cys Val Glu Ile Pro
            260
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<210> 43
<211> 259
<212> PRT
<213> Homo sapiens

<400> 43

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Met Tyr Val Leu Ser Pro Val Glu Phe Ile Ile Leu Gln Leu Leu Phe
 1                5                  10                  15
Ile Gln Ala Ile Ser Ser Ser Leu Lys Gly Phe Leu Ser Ala Met Arg
            20                  25                  30
Leu Ala His Arg Gly Cys Asn Val Asp Thr Pro Val Ser Thr Leu Thr
        35                  40                  45
Pro Val Lys Thr Ser Glu Phe Glu Asn Phe Lys Thr Lys Met Val Ile
    50                  55                  60
Thr Ser Lys Lys Asp Tyr Pro Leu Ser Lys Asn Phe Pro Tyr Ser Leu
65                  70                  75                  80
Glu His Leu Gln Thr Ser Tyr Cys Gly Leu Val Arg Val Asp Met Arg
                85                  90                  95
Met Leu Cys Leu Lys Ser Leu Arg Lys Leu Asp Leu Ser His Asn His
            100                 105                 110
Ile Lys Lys Leu Pro Ala Thr Ile Gly Asp Leu Ile His Leu Gln Glu
        115                 120                 125
Leu Asn Leu Asn Asp Asn His Leu Glu Ser Phe Ser Val Ala Leu Cys
    130                 135                 140
His Ser Thr Leu Gln Lys Ser Leu Arg Ser Leu Asp Leu Ser Lys Asn
145                 150                 155                 160
Lys Ile Lys Ala Leu Pro Val Gln Phe Cys Gln Leu Gln Glu Leu Lys
                165                 170                 175
Asn Leu Lys Leu Asp Asp Asn Glu Leu Ile Gln Phe Pro Cys Lys Ile
            180                 185                 190
Gly Gln Leu Ile Asn Leu Arg Phe Leu Ser Ala Ala Arg Asn Lys Leu
        195                 200                 205
Pro Phe Leu Pro Ser Glu Phe Arg Asn Leu Ser Leu Glu Tyr Leu Asp
    210                 215                 220
Leu Phe Gly Asn Thr Phe Glu Gln Pro Lys Val Leu Pro Val Ile Lys
225                 230                 235                 240
Leu Gln Ala Pro Leu Thr Leu Leu Glu Ser Ser Ala Arg Thr Ile Leu
                245                 250                 255
His Asn Arg
```

<210> 44
<211> 416
<212> PRT
<213> Homo sapiens

<400> 44

```
Met Lys Leu His Cys Glu Val Glu Val Ile Ser Arg His Leu Pro Ala
```

```
 1               5                  10                  15
Leu Gly Leu Arg Asn Arg Gly Lys Gly Val Arg Ala Val Leu Ser Leu
            20                  25                  30
Cys Gln Gln Thr Ser Arg Ser Gln Pro Pro Val Arg Ala Phe Leu Leu
        35                  40                  45
Ile Ser Thr Leu Lys Asp Lys Arg Gly Thr Arg Tyr Glu Leu Arg Glu
    50                  55                  60
Asn Ile Glu Gln Phe Phe Thr Lys Phe Val Asp Glu Gly Lys Ala Thr
65                  70                  75                  80
Val Arg Leu Lys Glu Pro Pro Val Asp Ile Cys Leu Ser Lys Ala Ile
                85                  90                  95
Ser Ser Ser Leu Lys Gly Phe Leu Ser Ala Met Arg Leu Ala His Arg
            100                 105                 110
Gly Cys Asn Val Asp Thr Pro Val Ser Thr Leu Thr Pro Val Lys Thr
        115                 120                 125
Ser Glu Phe Glu Asn Phe Lys Thr Lys Met Val Ile Thr Ser Lys Lys
    130                 135                 140
Asp Tyr Pro Leu Ser Lys Asn Phe Pro Tyr Ser Leu Glu His Leu Gln
145                 150                 155                 160
Thr Ser Tyr Cys Gly Leu Val Arg Val Asp Met Arg Met Leu Cys Leu
                165                 170                 175
Lys Ser Leu Arg Lys Leu Asp Leu Ser His Asn His Ile Lys Lys Leu
            180                 185                 190
Pro Ala Thr Ile Gly Asp Leu Ile His Leu Gln Glu Leu Asn Leu Asn
        195                 200                 205
Asp Asn His Leu Glu Ser Phe Ser Val Ala Leu Cys His Ser Thr Leu
    210                 215                 220
Gln Lys Ser Leu Arg Ser Leu Asp Leu Ser Lys Asn Lys Ile Lys Ala
225                 230                 235                 240
Leu Pro Val Gln Phe Cys Gln Leu Gln Glu Leu Lys Asn Leu Lys Leu
                245                 250                 255
Asp Asp Asn Glu Leu Ile Gln Phe Pro Cys Lys Ile Gly Gln Leu Ile
            260                 265                 270
Asn Leu Arg Phe Leu Ser Ala Ala Arg Asn Lys Leu Pro Phe Leu Pro
        275                 280                 285
Ser Glu Phe Arg Asn Leu Ser Leu Glu Tyr Leu Asp Leu Phe Gly Asn
    290                 295                 300
Thr Phe Glu Gln Pro Lys Val Leu Pro Val Ile Lys Leu Gln Ala Pro
305                 310                 315                 320
Leu Thr Leu Leu Glu Ser Ser Ala Arg Thr Ile Leu His Asn Arg Asn
                325                 330                 335
Arg Ile Pro Tyr Gly Ser His Ile Ile Pro Phe His Leu Cys Gln Asp
            340                 345                 350
Leu Asp Thr Ala Lys Ile Cys Val Cys Gly Arg Phe Cys Leu Asn Ser
        355                 360                 365
Phe Ile Gln Gly Thr Thr Thr Met Asn Leu His Ser Val Ala His Thr
    370                 375                 380
Val Val Leu Val Asp Asn Leu Gly Gly Thr Glu Ala Pro Ile Ile Ser
385                 390                 395                 400
Tyr Phe Cys Ser Leu Gly Cys Tyr Val Asn Ser Ser Asp Met Leu Lys
                405                 410                 415
```

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/19929

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :C07K 14/47; C12N 5/10, 5/16, 15/12, 15/63, 15/64
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350; 536/23.1, 23.5; 435/69.1, 71.1, 71.2, 325, 471, 320.1, 252.3, 254.11

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 92/05256 A1 (GENETICS INSTITUTE, INC., THE WISTAR INSTITUTE) 02 April 1992 (02/04/92), see entire document.	1-7

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 16 AUGUST 2001	Date of mailing of the international search report 09 NOV 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PREMA MERTZ Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/19929

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-7 (SEQ ID NO:1, 28)

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/19929

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

530/350; 536/23.1, 23.5; 435/69.1, 71.1, 71.2, 325, 471, 320.1, 252.3, 254.11

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Groups 1-22, claims 1-7, drawn to an isolated nucleic acid of SEQ ID NO X or a peptide of SEQ ID NO NO: Y, wherein X and Y are values that correlate to those listed in Table 1 on page 24, and correspond to one of the GSK Gene ID, respectively. For example,

If group I is elected, this correlates to Gene no 237168, of Table 1, wherein X is 1 and Y is 23.
If group 2 is elected, this correlates to Gene No 251170, of Table 1, wherein X is 2 and Y is 24.

The inventions listed as Groups 1-22 do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:
Pursuant to 37 C.F.R. § 1.475 (d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first-recited product, a nucleic acid of SEQ ID NO:1, encoding a protein of SEQ ID NO:23, a vector, a host cell, a method of making the protein of SEQ ID NO:23, and the protein of SEQ ID NO:23. Further pursuant to 37 C.F.R. § 1.475 (d), the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.